

601899, and in cited publications numbered 8742–8743 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcobalamin II; Macrocytic Anemia (TCN2, Accession NM_000355) is another VGAM927 host target gene. TCN2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCN2 BINDING SITE, designated SEQ ID:5916, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35018] Another function of VGAM927 is therefore inhibition of Transcobalamin II; Macrocytic Anemia (TCN2, Accession NM_000355). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCN2. Tec Protein Tyrosine Kinase (TEC, Accession NM_003215) is another VGAM927 host target gene. TEC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEC BINDING SITE, designated SEQ ID:9216, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35019] Another function of VGAM927 is therefore inhibition of Tec Protein Tyrosine Kinase (TEC, Accession NM_003215). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEC. AIG-1 (Accession NM_016108) is another VGAM927 host target gene. AIG-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AIG-1 BINDING SITE, designated SEQ ID:18190, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35020] Another function of VGAM927 is therefore inhibition of AIG-1 (Accession NM_016108). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AIG-1.

Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476) is another VGAM927 host target gene.

BTN2A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BTN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A1 BINDING SITE, designated SEQ ID:27804, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35021] Another function of VGAM927 is therefore inhibition of Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A1. FLJ10120 (Accession NM_018001) is another VGAM927 host target gene. FLJ10120 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10120 BINDING SITE, designated

SEQ ID:19728, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35022] Another function of VGAM927 is therefore inhibition of FLJ10120 (Accession NM_018001). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10120. FLJ10540 (Accession NM_018131) is another VGAM927 host target gene. FLJ10540 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10540 BINDING SITE, designated SEQ ID:19929, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35023] Another function of VGAM927 is therefore inhibition of FLJ10540 (Accession NM_018131). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10540. FLJ23045 (Accession NM_024704) is another VGAM927 host target gene. FLJ23045 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ23045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23045 BINDING SITE, designated SEQ ID:24020, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35024] Another function of VGAM927 is therefore inhibition of FLJ23045 (Accession NM_024704). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23045. KIAA1361 (Accession XM_030845) is another VGAM927 host target gene. KIAA1361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1361 BINDING SITE, designated SEQ ID:31169, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35025] Another function of VGAM927 is therefore inhibition of

KIAA1361 (Accession XM_030845). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1361. KIAA1750 (Accession XM_043067) is another VGAM927 host target gene. KIAA1750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1750 BINDING SITE, designated SEQ ID:33870, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35026] Another function of VGAM927 is therefore inhibition of KIAA1750 (Accession XM_043067). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1750. Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM_133177) is another VGAM927 host target gene. PTPRU BINDING SITE1 through PTPRU BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRU, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRU BINDING SITE1 through PTPRU BINDING SITE3, designated SEQ ID:28402, SEQ ID:28407 and SEQ ID:12257 respectively, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35027] Another function of VGAM927 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM_133177). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRU. LOC144962 (Accession XM_084990) is another VGAM927 host target gene. LOC144962 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144962 BINDING SITE, designated SEQ ID:37792, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35028] Another function of VGAM927 is therefore inhibition of

LOC144962 (Accession XM_084990). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144962. LOC151248 (Accession XM_087143) is another VGAM927 host target gene. LOC151248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151248 BINDING SITE, designated SEQ ID:39090, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35029] Another function of VGAM927 is therefore inhibition of LOC151248 (Accession XM_087143). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151248. LOC157421 (Accession XM_098756) is another VGAM927 host target gene. LOC157421 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC157421 BINDING SITE, designated SEQ ID:41795, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35030] Another function of VGAM927 is therefore inhibition of LOC157421 (Accession XM_098756). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157421. LOC158014 (Accession XM_088442) is another VGAM927 host target gene. LOC158014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158014 BINDING SITE, designated SEQ ID:39693, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35031] Another function of VGAM927 is therefore inhibition of LOC158014 (Accession XM_088442). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158014. LOC220846 (Accession XM_165515) is an-

other VGAM927 host target gene. LOC220846 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220846 BINDING SITE, designated SEQ ID:43663, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35032] Another function of VGAM927 is therefore inhibition of LOC220846 (Accession XM_165515). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220846. LOC220930 (Accession XM_167624) is another VGAM927 host target gene. LOC220930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220930 BINDING SITE, designated SEQ ID:44731, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35033] Another function of VGAM927 is therefore inhibition of LOC220930 (Accession XM_167624). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220930. LOC51320 (Accession NM_016626) is another VGAM927 host target gene. LOC51320 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51320 BINDING SITE, designated SEQ ID:18741, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35034] Another function of VGAM927 is therefore inhibition of LOC51320 (Accession NM_016626). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51320. LOC84549 (Accession NM_032509) is another VGAM927 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26261, to the nucleotide sequence of VGAM927 RNA, herein designated VGAM RNA, also designated SEQ ID:3638.

[35035] Another function of VGAM927 is therefore inhibition of LOC84549 (Accession NM_032509). Accordingly, utilities of VGAM927 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 928 (VGAM928) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35036] VGAM928 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM928 was detected is described hereinabove with reference to Figs. 1–8.

[35037] VGAM928 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM928 host target gene, herein

designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35038] VGAM928 gene encodes a VGAM928 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM928 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM928 precursor RNA is designated SEQ ID:914, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:914 is located at position 67062 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[35039] VGAM928 precursor RNA folds onto itself, forming VGAM928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35040] An enzyme complex designated DICER COMPLEX, `dices` the VGAM928 folded precursor RNA into VGAM928 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM928 RNA is designated SEQ ID:3639, and is provided hereinbelow with reference to the sequence listing part.

[35041] VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM928 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35042] VGAM928 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM928 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM928 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35043] The complementary binding of VGAM928 RNA, herein designated VGAM RNA, to host target binding sites on VGAM928 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM928 host target RNA into VGAM928 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[35044] It is appreciated that VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM928 host target genes. The mRNA of each one of this plurality of VGAM928 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM928 RNA, herein designated VGAM RNA, and which when bound by VGAM928 RNA causes inhibition of translation of respective one or more VGAM928 host target proteins.

[35045] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM928 gene, herein designated VGAM GENE, on one or more VGAM928 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35046] It is yet further appreciated that a function of VGAM928 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM928 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM928 correlate with, and may be deduced from, the identity of the host target genes which VGAM928 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35047] Nucleotide sequences of the VGAM928 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM928 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM928 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM928 are further described hereinbelow with reference to Table 1.

[35048] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM928 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM928 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35049] As mentioned hereinabove with reference to Fig. 1, a function of VGAM928 gene, herein designated VGAM is inhibition of expression of VGAM928 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM928 correlate with, and may be deduced from, the identity of the target genes which VGAM928 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35050] Secreted Frizzled-related Protein 4 (SFRP4, Accession NM_003014) is a VGAM928 host target gene. SFRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP4 BINDING SITE, designated SEQ ID:8938, to the nucleotide sequence of VGAM928 RNA, herein designated

VGAM RNA, also designated SEQ ID:3639.

[35051] A function of VGAM928 is therefore inhibition of Secreted Frizzled-related Protein 4 (SFRP4, Accession NM_003014). Accordingly, utilities of VGAM928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP4. ATP Synthase Mitochondrial F1 Complex Assembly Factor 2 (ATPAF2, Accession XM_058905) is another VGAM928 host target gene. ATPAF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATPAF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATPAF2 BINDING SITE, designated SEQ ID:36790, to the nucleotide sequence of VGAM928 RNA, herein designated VGAM RNA, also designated SEQ ID:3639.

[35052] Another function of VGAM928 is therefore inhibition of ATP Synthase Mitochondrial F1 Complex Assembly Factor 2 (ATPAF2, Accession XM_058905). Accordingly, utilities of VGAM928 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATPAF2. Fig. 1 further provides a conceptual description of a

novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 929 (VGAM929) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35053] VGAM929 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM929 was detected is described hereinabove with reference to Figs. 1–8.

[35054] VGAM929 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35055] VGAM929 gene encodes a VGAM929 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM929 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM929 precursor RNA is designated SEQ ID:915, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:915 is

located at position 64221 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[35056] VGAM929 precursor RNA folds onto itself, forming VGAM929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35057] An enzyme complex designated DICER COMPLEX, `dices` the VGAM929 folded precursor RNA into VGAM929 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM929 RNA is designated SEQ ID:3640, and is provided hereinbelow with reference to the sequence listing part.

[35058] VGAM929 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM929 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[35059] VGAM929 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM929 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM929 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM929 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35060] The complementary binding of VGAM929 RNA, herein designated VGAM RNA, to host target binding sites on VGAM929 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM929 host target RNA into VGAM929 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35061] It is appreciated that VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM929 host target genes. The mRNA of each one of this plurality of VGAM929 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM929 RNA, herein designated VGAM RNA, and which when bound by VGAM929 RNA causes inhibition of translation of respective one or more VGAM929

host target proteins.

[35062] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM929 gene, herein designated VGAM GENE, on one or more VGAM929 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35063] It is yet further appreciated that a function of VGAM929 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kid-

ney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM929 correlate with, and may be deduced from, the identity of the host target genes which VGAM929 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35064] Nucleotide sequences of the VGAM929 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM929 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM929 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM929 are further described hereinbelow with reference to Table 1.

[35065] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM929 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM929 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35066] As mentioned hereinabove with reference to Fig. 1, a function of VGAM929 gene, herein designated VGAM is inhibition of expression of VGAM929 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM929 correlate with, and may be deduced from, the identity of the target genes which VGAM929 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35067] Diphtheria Toxin Receptor (heparin-binding epidermal growth factor-like growth factor) (DTR, Accession NM_001945) is a VGAM929 host target gene. DTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTR BINDING SITE, designated SEQ ID:7661, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35068] A function of VGAM929 is therefore inhibition of Diphtheria Toxin Receptor (heparin-binding epidermal growth factor-like growth factor) (DTR, Accession NM_001945), a gene which may be involved in macrophage-mediated cellular proliferation. Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DTR. The function of DTR and its association with various diseases and clini-

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM242. Lysozyme (renal amyloidosis) (LYZ, Accession NM_000239) is another VGAM929 host target gene. LYZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LYZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LYZ BINDING SITE, designated SEQ ID:5756, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35069] Another function of VGAM929 is therefore inhibition of Lysozyme (renal amyloidosis) (LYZ, Accession NM_000239), a gene which a bacteriolytic enzyme. Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LYZ. The function of LYZ has been established by previous studies. Lysozyme (EC 3.2.1.17) catalyzes the hydrolysis of certain mucopolysaccharides of bacterial cell walls. Specifically, it catalyzes the hydrolysis of the bacterial cell wall beta(1-4) glycosidic linkages between N-acetylmuramic acid and N-acetylglucosamine. It

is found in spleen, lung, kidney, white blood cells, plasma, saliva, milk and tears. Alexander Fleming (1881–1955), of penicillin fame, discovered and named lysozyme. In a communication to the Royal Society, Fleming (1922) wrote: '..I wish to draw attention to a substance present in the tissues and secretions of the body, which is capable of rapidly dissolving certain bacteria. As this substance has properties akin to those of ferments I have called it a Lysozyme..' Fleming and Allison (1922) demonstrated an unusually high concentration in cartilage, indeed the highest of any tissue. Its role in cartilage is unknown. It resembles lactalbumin (OMIM Ref. No. 149750) in structure. Human lysozyme has a molecular mass of 14,602 Da. Neufeld (1972) suggested that a genetic defect of lysozyme might underlie a skeletal dysplasia. Spitznagel et al. (1972) observed a patient with selective deficiency of a particular type of neutrophil granule which resulted in about 50% reduction in lysozyme levels. The patient showed increased susceptibility to infection. Prieur et al. (1974) described inherited lysozyme deficiency in rabbits. No abnormality of cartilage or bone was noted (Greenwald et al., 1975). Older mutant rabbits showed increased susceptibility to infections, especially subcutaneous ab-

scesses (Prieur, 1975). Camara et al. (1990) identified 2 isozymes of rabbit lysozyme and showed that their distribution was tissue specific. Leukocytic and gastrointestinal isozymes were clearly distinguished, and a possible lymphoepithelial isozyme that resembled the gastrointestinal isozyme electrophoretically and chromatographically but not kinetically was demonstrated. Mutant, lysozyme-deficient rabbits completely lacked a detectable leukocytic isozyme but had gastrointestinal and lymphoepithelial isozymes indistinguishable from those of normal rabbits. By electrophoretic methods, the mutant rabbits were shown to lack a protein band corresponding to that of the leukocytic isozyme in normal rabbits Canet et al. (1999) studied the unfolding and refolding properties of human lysozyme and 2 of its amyloidogenic variants, ile56 to thr and asp67 to his, by stopped-flow fluorescence and hydrogen exchange pulse labeling coupled with mass spectrometry. Their results suggested that the amyloidogenic nature of the lysozyme variants arises from a decrease in the stability of the native fold relative to partially folded intermediates. The origin of this instability was different in the 2 variants, being caused in one case primarily by a reduction in the folding rate and in the other by an in-

crease in the unfolding rate. In both cases, this resulted in a low population of soluble partially folded species that can aggregate in a slow and controlled manner to form amyloid fibrils

[35070] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35071] Canet, D.; Sunde, M.; Last, A. M.; Miranker, A.; Spencer, A.; Robinson, C. V.; Dobson, C. M. : Mechanistic studies of the folding of human lysozyme and the origin of amyloidogenic behavior in its disease-related variants. *Biochemistry* 38: 6419–6427, 1999. ; and

[35072] Camara, V. M.; Harding, J. W.; Prieur, D. J. : Inherited lysozyme deficiency in rabbits: the absence of a primary isozyme of lysozyme as the cause of the condition. *Lab. Invest.* 63: 544–55.

[35073] Further studies establishing the function and utilities of LYZ are found in John Hopkins OMIM database record ID 153450, and in cited publications numbered 668–67 and 5245 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RNA (guanine–7–) Methyltransferase (RNMT, Accession NM_003799) is another VGAM929 host target gene. RNMT

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9886, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35074] Another function of VGAM929 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.FLJ14166 (Accession NM_024565) is another VGAM929 host target gene. FLJ14166 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ14166 BINDING SITE, designated SEQ ID:23790, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35075] Another function of VGAM929 is therefore inhibition of FLJ14166 (Accession NM_024565). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14166. GRB2-associated Binding Protein 3 (GAB3, Accession NM_080612) is another VGAM929 host target gene. GAB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB3 BINDING SITE, designated SEQ ID:27927, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35076] Another function of VGAM929 is therefore inhibition of GRB2-associated Binding Protein 3 (GAB3, Accession NM_080612). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB3. KIAA1223 (Accession

XM_048747) is another VGAM929 host target gene.

KIAA1223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1223 BINDING SITE, designated SEQ ID:35246, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35077] Another function of VGAM929 is therefore inhibition of KIAA1223 (Accession XM_048747). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. Leiomodin 1 (smooth muscle) (LMOD1, Accession NM_012134) is another VGAM929 host target gene. LMOD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LMOD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMOD1 BINDING SITE, designated SEQ ID:14444, to the nucleotide sequence of VGAM929 RNA,

herein designated VGAM RNA, also designated SEQ ID:3640.

[35078] Another function of VGAM929 is therefore inhibition of Leiomodin 1 (smooth muscle) (LMOD1, Accession NM_012134). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMOD1. Stromal Antigen 2 (STAG2, Accession XM_047285) is another VGAM929 host target gene. STAG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAG2 BINDING SITE, designated SEQ ID:34929, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35079] Another function of VGAM929 is therefore inhibition of Stromal Antigen 2 (STAG2, Accession XM_047285). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAG2. LOC115129 (Accession XM_055292) is another VGAM929 host target gene. LOC115129 BIND-

ING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36250, to the nucleotide sequence of VGAM929 RNA, herein designated VGAM RNA, also designated SEQ ID:3640.

[35080] Another function of VGAM929 is therefore inhibition of LOC115129 (Accession XM_055292). Accordingly, utilities of VGAM929 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 930 (VGAM930) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35081] VGAM930 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM930 was detected is described hereinabove with reference to Figs. 1-8.

[35082] VGAM930 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Amsacta Moorei Entomopoxvirus. VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35083] VGAM930 gene encodes a VGAM930 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM930 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM930 precursor RNA is designated SEQ ID:916, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:916 is located at position 48640 relative to the genome of Amsacta Moorei Entomopoxvirus.

[35084] VGAM930 precursor RNA folds onto itself, forming VGAM930 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[35085] An enzyme complex designated DICER COMPLEX, `dices` the VGAM930 folded precursor RNA into VGAM930 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM930 RNA is designated SEQ ID:3641, and is provided hereinbelow with reference to the sequence listing part.

[35086] VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM930 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35087] VGAM930 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM930 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM930 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM930 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35088] The complementary binding of VGAM930 RNA, herein designated VGAM RNA, to host target binding sites on VGAM930 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM930 host target RNA into VGAM930 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35089] It is appreciated that VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM930 host target genes. The mRNA of each one of this plurality of VGAM930 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM930 RNA, herein designated VGAM RNA, and which when bound by VGAM930 RNA causes inhibition of translation of respective one or more VGAM930 host target proteins.

[35090] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM930 gene, herein designated VGAM GENE, on one or more VGAM930 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35091] It is yet further appreciated that a function of VGAM930 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of viral infection by Amsacta Moorei Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM930 correlate with, and may be deduced from, the identity of the host target genes which VGAM930 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35092] Nucleotide sequences of the VGAM930 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM930 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM930 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM930 are further described hereinbelow with reference to Table 1.

[35093] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM930 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM930 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35094] As mentioned hereinabove with reference to Fig. 1, a function of VGAM930 gene, herein designated VGAM is inhibition of expression of VGAM930 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM930 correlate with, and may be deduced from, the identity of the target genes which VGAM930 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35095] FLJ13391 (Accession NM_032181) is a VGAM930 host target gene. FLJ13391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ13391 BINDING SITE, designated SEQ ID:25895, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35096] A function of VGAM930 is therefore inhibition of FLJ13391 (Accession NM_032181). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13391. KIAA0783 (Accession NM_014660) is another VGAM930 host target gene. KIAA0783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0783 BINDING SITE, designated SEQ ID:16104, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35097] Another function of VGAM930 is therefore inhibition of KIAA0783 (Accession NM_014660). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0783. KIAA1209 (Accession XM_027307) is another

VGAM930 host target gene. KIAA1209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1209 BINDING SITE, designated SEQ ID:30470, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35098] Another function of VGAM930 is therefore inhibition of KIAA1209 (Accession XM_027307). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1209. NX-17 (Accession NM_020665) is another VGAM930 host target gene. NX-17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NX-17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NX-17 BINDING SITE, designated SEQ ID:21834, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35099] Another function of VGAM930 is therefore inhibition of NX-17 (Accession NM_020665). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NX-17. PV1 (Accession NM_031310) is another VGAM930 host target gene. PV1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PV1 BINDING SITE, designated SEQ ID:25347, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35100] Another function of VGAM930 is therefore inhibition of PV1 (Accession NM_031310). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PV1. LOC153277 (Accession XM_098346) is another VGAM930 host target gene. LOC153277 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153277 BINDING SITE, designated SEQ ID:41603, to the nucleotide sequence of VGAM930 RNA, herein designated VGAM RNA, also designated SEQ ID:3641.

[35101] Another function of VGAM930 is therefore inhibition of LOC153277 (Accession XM_098346). Accordingly, utilities of VGAM930 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153277. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 931 (VGAM931) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35102] VGAM931 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM931 was detected is described hereinabove with reference to Figs. 1-8.

[35103] VGAM931 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African Swine Fever Virus. VGAM931 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35104] VGAM931 gene encodes a VGAM931 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM931 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM931 precursor RNA is designated SEQ ID:917, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:917 is located at position 133625 relative to the genome of African Swine Fever Virus.

[35105] VGAM931 precursor RNA folds onto itself, forming VGAM931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35106] An enzyme complex designated DICER COMPLEX, `dices` the VGAM931 folded precursor RNA into VGAM931 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM931 RNA is designated SEQ ID:3642, and is provided hereinbelow with reference to the sequence listing part.

[35107] VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM931 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35108] VGAM931 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM931 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM931 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35109] The complementary binding of VGAM931 RNA, herein designated VGAM RNA, to host target binding sites on VGAM931 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM931 host target RNA into VGAM931 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[35110] It is appreciated that VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM931 host target genes. The mRNA of each one of this plurality of VGAM931 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM931 RNA, herein designated VGAM RNA, and which when bound by VGAM931 RNA causes inhibition of translation of respective one or more VGAM931 host target proteins.

[35111] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM931 gene, herein designated VGAM GENE, on one or more VGAM931 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35112] It is yet further appreciated that a function of VGAM931 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGAM931 correlate with, and may be deduced from, the identity of the host target genes which VGAM931 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35113] Nucleotide sequences of the VGAM931 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM931 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM931 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM931 are further described hereinbelow with reference to Table 1.

[35114] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM931 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM931 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35115] As mentioned hereinabove with reference to Fig. 1, a function of VGAM931 gene, herein designated VGAM is inhibition of expression of VGAM931 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM931 correlate with, and may be deduced from, the identity of the target genes which VGAM931 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35116] FCRH1 (Accession NM_052938) is a VGAM931 host target gene. FCRH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCRH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCRH1 BINDING SITE, designated SEQ ID:27497, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ

ID:3642.

[35117] A function of VGAM931 is therefore inhibition of FCRH1 (Accession NM_052938). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCRH1. Inhibitor of DNA Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM_001546) is another VGAM931 host target gene. ID4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ID4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ID4 BINDING SITE, designated SEQ ID:7271, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35118] Another function of VGAM931 is therefore inhibition of Inhibitor of DNA Binding 4, Dominant Negative Helix-loop-helix Protein (ID4, Accession NM_001546), a gene which negatively regulates cell differentiation. Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ID4. The function of ID4 has been established by

previous studies. Transcription factors containing a basic helix–loop–helix (bHLH) motif regulate the expression of tissue–specific genes in a number of mammalian and insect systems (Pagliuca et al., 1995). DNA–binding activity of the bHLH proteins is dependent on formation of homo– and/or heterodimers. Dominant–negative HLH proteins (encoded by Id–related genes) also contain the HLH–dimerization domain but lack the DNA–binding basic domain. Consequently, Id proteins inhibit binding to DNA and transcriptional transactivation by heterodimerization with bHLH proteins. Pagliuca et al. (1995) reported the cDNA sequence of a novel human HLH gene, to which the symbol ID4 was assigned, which lacks the basic domain. ID4 is differentially expressed in adult organs as 4 mRNA molecules that are presumably the result of differential splicing and/or alternative polyadenylation sites. Transfection experiments indicated that enforced expression of the ID4 protein inhibits the transactivation of the muscle creatine kinase (CKM; 123310) E–box enhancer by MyoD (MYOD1; 159970). By fluorescence in situ hybridization (FISH), Pagliuca et al. (1995) mapped the ID4 gene to 6p22–p21.3. By the same method, Rigolet et al. (1998) mapped the gene to 6p23–p22.3. For other dominant–neg–

active inhibitors of DNA binding, see ID1 (OMIM Ref. No. 600349), ID2 (OMIM Ref. No. 600386), and ID3 (600277

[35119] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35120] Pagliuca, A.; Bartoli, P. C.; Saccone, S.; Valle, G. D.; Lania, L. : Molecular cloning of ID4, a novel dominant negative helix-loop-helix human gene on chromosome 6p21.3-p22. Genomics 27: 200-203, 1995. ; and

[35121] Rigolet, M.; Rich, T.; Gross-Morand, M.-S.; Molina-Gomes, D.; Viegas-Pequignot, E.; Junien, C. : cDNA cloning, tissue distribution and chromosomal localization of the human ID4 gene. DNA.

[35122] Further studies establishing the function and utilities of ID4 are found in John Hopkins OMIM database record ID 600581, and in cited publications numbered 10185-10186 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Alpha 1 (PCDHA1, Accession NM_018900) is another VGAM931 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:20863 and SEQ ID:25382 respectively, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35123] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_018900). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_031860) is another VGAM931 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:25614 and SEQ ID:20883 respectively, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35124] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_031860). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM931 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20904, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35125] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM_018905) is another VGAM931 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20914, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35126] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM_018905). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM931 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20924, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35127] Another function of VGAM931 is therefore inhibition of

Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM931 host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20934, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35128] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM_018908) is another VGAM931 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20944, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35129] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM_018908). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM_031849) is another VGAM931 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:25586 and SEQ ID:20954 respectively, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35130] Another function of VGAM931 is therefore inhibition of

Protocadherin Alpha 6 (PCDHA6, Accession NM_031849). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM_018911) is another VGAM931 host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20974, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35131] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 8 (PCDHA8, Accession NM_018911). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM931 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25599, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35132] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM931 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated

SEQ ID:20843, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35133] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899) is another VGAM931 host target gene. PCDHAC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC2 BINDING SITE, designated SEQ ID:20853, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35134] Another function of VGAM931 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. Protocadherin

Beta 16 (PCDHB16, Accession NM_020957) is another VGAM931 host target gene. PCDHB16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB16 BINDING SITE, designated SEQ ID:21944, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35135] Another function of VGAM931 is therefore inhibition of Protocadherin Beta 16 (PCDHB16, Accession NM_020957), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB16. The function of PCDHB16 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHB16 is a member of the beta cluster of protocadherin genes on 5q31. For specific information on the PCDHB genes, see 604967. Using PCR with degenerate

primers to screen melanoma cell lines, Matsuyoshi et al. (1997) obtained a cDNA fragment encoding part of PCDHB16, which they termed ME1. RT-PCR analysis detected expression of ME1 in melanoma cell lines and normal fibroblast cell lines, but not in a squamous carcinoma cell lines or normal melanocytes, suggesting that ME1 may play a role in the strong cell-cell adhesiveness of melanoma cells.

[35136] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35137] Matsuyoshi, N.; Tanaka, T.; Toda, K.; Imamura, S. : Identification of novel cadherins expressed in human melanoma cells. J. Invest. Derm. 108: 908–913, 1997. ; and

[35138] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse and.

[35139] Further studies establishing the function and utilities of PCDHB16 are found in John Hopkins OMIM database record ID 606345, and in cited publications numbered 4514, 673 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence. Zinc Finger Protein 268 (ZNF268, Accession XM_031851) is another VGAM931 host target gene. ZNF268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF268 BINDING SITE, designated SEQ ID:31499, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35140] Another function of VGAM931 is therefore inhibition of Zinc Finger Protein 268 (ZNF268, Accession XM_031851). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF268. Chromosome 2 Open Reading Frame 6 (C2orf6, Accession NM_018221) is another VGAM931 host target gene. C2orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C2orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C2orf6 BINDING SITE,

designated SEQ ID:20141, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35141] Another function of VGAM931 is therefore inhibition of Chromosome 2 Open Reading Frame 6 (C2orf6, Accession NM_018221). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C2orf6. FLJ20086 (Accession NM_017661) is another VGAM931 host target gene. FLJ20086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20086 BINDING SITE, designated SEQ ID:19191, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35142] Another function of VGAM931 is therefore inhibition of FLJ20086 (Accession NM_017661). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20086. FLJ20220 (Accession NM_017718) is another VGAM931

host target gene. FLJ20220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20220 BINDING SITE, designated SEQ ID:19302, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35143] Another function of VGAM931 is therefore inhibition of FLJ20220 (Accession NM_017718). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20220. FLJ20436 (Accession NM_017822) is another VGAM931 host target gene. FLJ20436 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20436, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20436 BINDING SITE, designated SEQ ID:19473, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35144] Another function of VGAM931 is therefore inhibition of FLJ20436 (Accession NM_017822). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20436. Interleukin 18 Binding Protein (IL18BP, Accession NM_005699) is another VGAM931 host target gene. IL18BP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL18BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL18BP BINDING SITE, designated SEQ ID:12250, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35145] Another function of VGAM931 is therefore inhibition of Interleukin 18 Binding Protein (IL18BP, Accession NM_005699). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL18BP. KIAA1219 (Accession XM_028835) is another VGAM931 host target gene. KIAA1219 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by KIAA1219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1219 BINDING SITE, designated SEQ ID:30757, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35146] Another function of VGAM931 is therefore inhibition of KIAA1219 (Accession XM_028835). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1219. KIAA1884 (Accession XM_055539) is another VGAM931 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36293, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35147] Another function of VGAM931 is therefore inhibition of KIAA1884 (Accession XM_055539). Accordingly, utilities

of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. PDP (Accession NM_018444) is another VGAM931 host target gene. PDP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDP BINDING SITE, designated SEQ ID:20514, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35148] Another function of VGAM931 is therefore inhibition of PDP (Accession NM_018444). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDP. SET Binding Protein 1 (SETBP1, Accession NM_015559) is another VGAM931 host target gene. SETBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SETBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SETBP1 BIND-

ING SITE, designated SEQ ID:17824, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35149] Another function of VGAM931 is therefore inhibition of SET Binding Protein 1 (SETBP1, Accession NM_015559). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SETBP1. LOC150358 (Accession XM_097842) is another VGAM931 host target gene. LOC150358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150358 BINDING SITE, designated SEQ ID:41158, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35150] Another function of VGAM931 is therefore inhibition of LOC150358 (Accession XM_097842). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150358. LOC155081 (Accession XM_088145) is an-

other VGAM931 host target gene. LOC155081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155081 BINDING SITE, designated SEQ ID:39543, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35151] Another function of VGAM931 is therefore inhibition of LOC155081 (Accession XM_088145). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155081. LOC157280 (Accession XM_058301) is another VGAM931 host target gene. LOC157280 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157280 BINDING SITE, designated SEQ ID:36594, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35152] Another function of VGAM931 is therefore inhibition of LOC157280 (Accession XM_058301). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157280. LOC202802 (Accession XM_114560) is another VGAM931 host target gene. LOC202802 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202802 BINDING SITE, designated SEQ ID:42988, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35153] Another function of VGAM931 is therefore inhibition of LOC202802 (Accession XM_114560). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202802. LOC219401 (Accession XM_166706) is another VGAM931 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44589, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35154] Another function of VGAM931 is therefore inhibition of LOC219401 (Accession XM_166706). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC221543 (Accession XM_168091) is another VGAM931 host target gene. LOC221543 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221543, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221543 BINDING SITE, designated SEQ ID:45011, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35155] Another function of VGAM931 is therefore inhibition of LOC221543 (Accession XM_168091). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221543. LOC222228 (Accession XM_168627) is another VGAM931 host target gene. LOC222228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222228 BINDING SITE, designated SEQ ID:45274, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35156] Another function of VGAM931 is therefore inhibition of LOC222228 (Accession XM_168627). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222228. LOC222233 (Accession XM_168560) is another VGAM931 host target gene. LOC222233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222233 BINDING SITE, designated SEQ ID:45243, to the nucleotide sequence of VGAM931 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3642.

[35157] Another function of VGAM931 is therefore inhibition of LOC222233 (Accession XM_168560). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222233. LOC254018 (Accession XM_173066) is another VGAM931 host target gene. LOC254018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254018 BINDING SITE, designated SEQ ID:46318, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35158] Another function of VGAM931 is therefore inhibition of LOC254018 (Accession XM_173066). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254018. LOC255448 (Accession XM_170623) is another VGAM931 host target gene. LOC255448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255448, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255448 BINDING SITE, designated SEQ ID:45404, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35159] Another function of VGAM931 is therefore inhibition of LOC255448 (Accession XM_170623). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255448. LOC257596 (Accession XM_175296) is another VGAM931 host target gene. LOC257596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257596 BINDING SITE, designated SEQ ID:46752, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35160] Another function of VGAM931 is therefore inhibition of LOC257596 (Accession XM_175296). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC257596. LOC91308 (Accession XM_037600) is another VGAM931 host target gene. LOC91308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91308 BINDING SITE, designated SEQ ID:32655, to the nucleotide sequence of VGAM931 RNA, herein designated VGAM RNA, also designated SEQ ID:3642.

[35161] Another function of VGAM931 is therefore inhibition of LOC91308 (Accession XM_037600). Accordingly, utilities of VGAM931 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91308. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 932 (VGAM932) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35162] VGAM932 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM932 was detected is described hereinabove with reference to Figs. 1–8.

[35163] VGAM932 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35164] VGAM932 gene encodes a VGAM932 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM932 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM932 precursor RNA is designated SEQ ID:918, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:918 is located at position 122063 relative to the genome of Human Herpesvirus 4.

[35165] VGAM932 precursor RNA folds onto itself, forming VGAM932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35166] An enzyme complex designated DICER COMPLEX, `dices` the VGAM932 folded precursor RNA into VGAM932 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM932 RNA is designated SEQ ID:3643, and is provided hereinbelow with reference to the sequence listing part.

[35167] VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM932 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35168] VGAM932 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM932 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM932 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35169] The complementary binding of VGAM932 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM932 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM932 host target RNA into VGAM932 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35170] It is appreciated that VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM932 host target genes. The mRNA of each one of this plurality of VGAM932 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM932 RNA, herein designated VGAM RNA, and which when bound by VGAM932 RNA causes inhibition of translation of respective one or more VGAM932 host target proteins.

[35171] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM932 gene, herein designated VGAM GENE, on one or more VGAM932 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35172] It is yet further appreciated that a function of VGAM932 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM932 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM932 correlate with, and may be deduced from, the identity of the host target genes which VGAM932 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35173] Nucleotide sequences of the VGAM932 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

5' duced 5' VGAM932 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM932 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM932 are further described hereinbelow with reference to Table 1.

[35174] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM932 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM932 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35175] As mentioned hereinabove with reference to Fig. 1, a function of VGAM932 gene, herein designated VGAM is inhibition of expression of VGAM932 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM932 correlate with, and may be deduced from, the identity of the target genes which VGAM932 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35176] PIF1 (Accession XM_027898) is a VGAM932 host target gene. PIF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PIF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIF1 BINDING SITE, designated SEQ ID:30585, to the nucleotide sequence of VGAM932 RNA, herein designated VGAM RNA, also designated SEQ ID:3643.

[35177] A function of VGAM932 is therefore inhibition of PIF1 (Accession XM_027898). Accordingly, utilities of VGAM932 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIF1. SE57-1 (Accession NM_025214) is another VGAM932 host target gene. SE57-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SE57-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SE57-1 BINDING SITE, designated SEQ ID:24888, to the nucleotide sequence of VGAM932 RNA, herein designated VGAM RNA, also designated SEQ ID:3643.

[35178] Another function of VGAM932 is therefore inhibition of SE57-1 (Accession NM_025214). Accordingly, utilities of VGAM932 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SE57-1.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 933 (VGAM933) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35179] VGAM933 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM933 was detected is described hereinabove with reference to Figs. 1-8.

[35180] VGAM933 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35181] VGAM933 gene encodes a VGAM933 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM933 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM933 precursor RNA is designated SEQ ID:919, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:919 is located at position 123567 relative to the genome of Human Herpesvirus 4.

[35182] VGAM933 precursor RNA folds onto itself, forming VGAM933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35183] An enzyme complex designated DICER COMPLEX, `dices` the VGAM933 folded precursor RNA into VGAM933 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM933 RNA is designated SEQ ID:3644, and is provided hereinbelow with reference to the sequence listing part.

[35184] VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM933 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35185] VGAM933 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM933 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM933 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35186] The complementary binding of VGAM933 RNA, herein designated VGAM RNA, to host target binding sites on VGAM933 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM933 host target RNA into VGAM933 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35187] It is appreciated that VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM933 host target genes. The mRNA of each one of this plurality of VGAM933 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM933 RNA, herein designated VGAM RNA, and which when bound by VGAM933 RNA causes in-

hibition of translation of respective one or more VGAM933 host target proteins.

[35188] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM933 gene, herein designated VGAM GENE, on one or more VGAM933 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35189] It is yet further appreciated that a function of VGAM933 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM933 include diagnosis, prevention and

treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM933 correlate with, and may be deduced from, the identity of the host target genes which VGAM933 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35190] Nucleotide sequences of the VGAM933 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM933 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM933 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM933 are further described hereinbelow with reference to Table 1.

[35191] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM933 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM933 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35192] As mentioned hereinabove with reference to Fig. 1, a function of VGAM933 gene, herein designated VGAM is inhibition of expression of VGAM933 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM933 correlate with, and may be deduced from, the identity of the target genes which VGAM933 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35193] Ectonucleoside Triphosphate Diphosphohydrolase 6 (putative function) (ENTPD6, Accession NM_001247) is a VGAM933 host target gene. ENTPD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENTPD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENTPD6 BINDING SITE, designated SEQ ID:6917, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35194] A function of VGAM933 is therefore inhibition of Ectonucleoside Triphosphate Diphosphohydrolase 6 (putative function) (ENTPD6, Accession NM_001247), a gene which might support glycosylation reactions in the golgi apparatus and, when released from cells, might catalyze the hydrolysis of extracellular nucleotides. Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ENTPD6. The function of ENTPD6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177) is another VGAM933 host target gene. C17orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf26 BINDING SITE, designated SEQ ID:29185, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35195] Another function of VGAM933 is therefore inhibition of Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf26. FLJ13265 (Accession NM_024877) is another VGAM933 host target gene. FLJ13265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ13265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13265 BINDING SITE, designated SEQ ID:24311, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35196] Another function of VGAM933 is therefore inhibition of FLJ13265 (Accession NM_024877). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13265. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962) is another VGAM933 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30973, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35197] Another function of VGAM933 is therefore inhibition of

Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA1493 (Accession XM_034415) is another VGAM933 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32092, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35198] Another function of VGAM933 is therefore inhibition of KIAA1493 (Accession XM_034415). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. LOC113230 (Accession XM_053966) is another VGAM933 host target gene. LOC113230 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC113230, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113230 BINDING SITE, designated SEQ ID:36131, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35199] Another function of VGAM933 is therefore inhibition of LOC113230 (Accession XM_053966). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113230. LOC115399 (Accession XM_055874) is another VGAM933 host target gene. LOC115399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115399 BINDING SITE, designated SEQ ID:36347, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35200] Another function of VGAM933 is therefore inhibition of LOC115399 (Accession XM_055874). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC115399. LOC147817 (Accession XM_085903) is another VGAM933 host target gene. LOC147817 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147817 BINDING SITE, designated SEQ ID:38387, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35201] Another function of VGAM933 is therefore inhibition of LOC147817 (Accession XM_085903). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147817. LOC148147 (Accession XM_086071) is another VGAM933 host target gene. LOC148147 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148147 BINDING SITE, designated SEQ ID:38474, to the nucleotide sequence of VGAM933 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3644.

[35202] Another function of VGAM933 is therefore inhibition of LOC148147 (Accession XM_086071). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148147. LOC163412 (Accession XM_088868) is another VGAM933 host target gene. LOC163412 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163412, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163412 BINDING SITE, designated SEQ ID:39953, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35203] Another function of VGAM933 is therefore inhibition of LOC163412 (Accession XM_088868). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163412. LOC58525 (Accession XM_086045) is another VGAM933 host target gene. LOC58525 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC58525, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58525 BINDING SITE, designated SEQ ID:38457, to the nucleotide sequence of VGAM933 RNA, herein designated VGAM RNA, also designated SEQ ID:3644.

[35204] Another function of VGAM933 is therefore inhibition of LOC58525 (Accession XM_086045). Accordingly, utilities of VGAM933 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58525. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 934 (VGAM934) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35205] VGAM934 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM934 was detected is described hereinabove with reference to Figs. 1–8.

[35206] VGAM934 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4.

VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35207] VGAM934 gene encodes a VGAM934 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM934 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM934 precursor RNA is designated SEQ ID:920, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:920 is located at position 123384 relative to the genome of Human Herpesvirus 4.

[35208] VGAM934 precursor RNA folds onto itself, forming VGAM934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35209] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM934 folded precursor RNA into VGAM934 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM934 RNA is designated SEQ ID:3645, and is provided hereinbelow with reference to the sequence listing part.

[35210] VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM934 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35211] VGAM934 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM934 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM934 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35212] The complementary binding of VGAM934 RNA, herein designated VGAM RNA, to host target binding sites on VGAM934 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM934 host target RNA into VGAM934 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35213] It is appreciated that VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM934 host target genes. The mRNA of each one of this plurality of VGAM934 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM934 RNA, herein designated VGAM RNA, and which when bound by VGAM934 RNA causes inhibition of translation of respective one or more VGAM934 host target proteins.

[35214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM934 gene, herein designated VGAM GENE, on one or more VGAM934 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35215] It is yet further appreciated that a function of VGAM934 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM934 correlate with, and may be deduced from, the identity of the host target genes which VGAM934 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35216] Nucleotide sequences of the VGAM934 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM934 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM934 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM934 are further described hereinbelow with reference to Table 1.

[35217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM934 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM934 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35218] As mentioned hereinabove with reference to Fig. 1, a function of VGAM934 gene, herein designated VGAM is inhibition of expression of VGAM934 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM934 correlate with, and may be deduced from, the identity of the target genes which VGAM934 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35219] Splicing Factor 1 (SF1, Accession NM_004630) is a VGAM934 host target gene. SF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SF1 BINDING SITE, designated SEQ ID:11003, to the nucleotide sequence of

VGAM934 RNA, herein designated VGAM RNA, also designated SEQ ID:3645.

[35220] A function of VGAM934 is therefore inhibition of Splicing Factor 1 (SF1, Accession NM_004630), a gene which is a transcriptional repressor and splicing factor. Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SF1. The function of SF1 has been established by previous studies. Toda et al. (1994) isolated a gene, designated ZFM1 by them, from cosmids from the MEN1 (OMIM Ref. No. 131100) region of 11q13 using exon amplification. They then obtained cDNAs from cerebral, cerebellar, and fetal liver libraries. The predicted 623-amino acid protein contains a nuclear transport domain, a metal-binding or zinc finger motif, and glutamine- and proline-rich regions. It shows some sequence similarity to WT1 (OMIM Ref. No. 607102) and EGR2 (OMIM Ref. No. 129010). RT-PCR was used to show expression in the thyroid gland, pancreas, adrenal gland, and ovary. By differential screening of a cDNA library obtained from GMCSF (OMIM Ref. No. 138960)-stimulated human myeloid leukemia cells, Caslini et al. (1997) cloned 2 additional isoforms of the ZNF162 gene, designated B3 and B4, that

encode 571- and 639-amino acid proteins, respectively. All of the ZNF162 isoforms contain a KH domain, a sequence motif present in proteins playing a major role in regulating cellular RNA metabolism.

[35221] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35222] Toda, T.; Iida, A.; Miwa, T.; Nakamura, Y.; Imai, T. : Isolation and characterization of a novel gene encoding nuclear protein at a locus (D11S636) tightly linked to multiple endocrine neoplasia type 1 (MEN1). Hum. Molec. Genet. 3: 465-470, 1994. ; and

[35223] Caslini, C.; Spinelli, O.; Cazzaniga, G.; Golay, J.; De Gioia, L.; Pedretti, A.; Breviario, F.; Amaru, R.; Barbui, T.; Biondi, A.; Introna, M.; Rambaldi, A. : Identification of two novel is.

[35224] Further studies establishing the function and utilities of SF1 are found in John Hopkins OMIM database record ID 601516, and in cited publications numbered 2776, 398 and 6654 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ22002 (Accession NM_024838) is another VGAM934 host target gene. FLJ22002 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by FLJ22002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22002 BINDING SITE, designated SEQ ID:24244, to the nucleotide sequence of VGAM934 RNA, herein designated VGAM RNA, also designated SEQ ID:3645.

[35225] Another function of VGAM934 is therefore inhibition of FLJ22002 (Accession NM_024838). Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22002. Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635) is another VGAM934 host target gene. P2RX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by P2RX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RX1 BINDING SITE, designated SEQ ID:33349, to the nucleotide sequence of VGAM934 RNA, herein designated VGAM RNA, also designated SEQ ID:3645.

[35226] Another function of VGAM934 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635). Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RX1. LOC255598 (Accession XM_173715) is another VGAM934 host target gene. LOC255598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255598 BINDING SITE, designated SEQ ID:46558, to the nucleotide sequence of VGAM934 RNA, herein designated VGAM RNA, also designated SEQ ID:3645.

[35227] Another function of VGAM934 is therefore inhibition of LOC255598 (Accession XM_173715). Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255598. LOC257103 (Accession XM_170982) is another VGAM934 host target gene. LOC257103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257103, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257103 BINDING SITE, designated SEQ ID:45753, to the nucleotide sequence of VGAM934 RNA, herein designated VGAM RNA, also designated SEQ ID:3645.

[35228] Another function of VGAM934 is therefore inhibition of LOC257103 (Accession XM_170982). Accordingly, utilities of VGAM934 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257103. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 935 (VGAM935) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35229] VGAM935 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM935 was detected is described hereinabove with reference to Figs. 1–8.

[35230] VGAM935 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Melanoplus Sanguinipes*

Entomopoxvirus. VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35231] VGAM935 gene encodes a VGAM935 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM935 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM935 precursor RNA is designated SEQ ID:921, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:921 is located at position 137342 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[35232] VGAM935 precursor RNA folds onto itself, forming VGAM935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35233] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM935 folded precursor RNA into VGAM935 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM935 RNA is designated SEQ ID:3646, and is provided hereinbelow with reference to the sequence listing part.

[35234] VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM935 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35235] VGAM935 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM935 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM935 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35236] The complementary binding of VGAM935 RNA, herein designated VGAM RNA, to host target binding sites on VGAM935 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM935 host target RNA into VGAM935 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35237] It is appreciated that VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM935 host target genes. The mRNA of each one of this plurality of VGAM935 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM935 RNA, herein designated VGAM RNA, and which when bound by VGAM935 RNA causes inhibition of translation of respective one or more VGAM935 host target proteins.

[35238] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM935 gene, herein designated VGAM GENE, on one or more VGAM935 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35239] It is yet further appreciated that a function of VGAM935 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM935 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM935 correlate with, and may be deduced from, the identity of the host target genes which VGAM935 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35240] Nucleotide sequences of the VGAM935 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM935 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM935 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM935 are further described hereinbelow with reference to Table 1.

[35241] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM935 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM935 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35242] As mentioned hereinabove with reference to Fig. 1, a function of VGAM935 gene, herein designated VGAM is inhibition of expression of VGAM935 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM935 correlate with, and may be deduced from, the identity of the target genes which VGAM935 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35243] Translocase of Inner Mitochondrial Membrane 8 Homolog A (yeast) (TIMM8A, Accession NM_004085) is a VGAM935 host target gene. TIMM8A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIMM8A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMM8A BINDING SITE,

designated SEQ ID:10289, to the nucleotide sequence of VGAM935 RNA, herein designated VGAM RNA, also designated SEQ ID:3646.

[35244] A function of VGAM935 is therefore inhibition of Translocase of Inner Mitochondrial Membrane 8 Homolog A (yeast) (TIMM8A, Accession NM_004085). Accordingly, utilities of VGAM935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMM8A. BDG-29 (Accession XM_051343) is another VGAM935 host target gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35813, to the nucleotide sequence of VGAM935 RNA, herein designated VGAM RNA, also designated SEQ ID:3646.

[35245] Another function of VGAM935 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of VGAM935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BDG-29. Chromosome 1 Open Reading Frame 26 (C1orf26, Acces-

sion NM_017673) is another VGAM935 host target gene. C1orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf26 BINDING SITE, designated SEQ ID:19217, to the nucleotide sequence of VGAM935 RNA, herein designated VGAM RNA, also designated SEQ ID:3646.

[35246] Another function of VGAM935 is therefore inhibition of Chromosome 1 Open Reading Frame 26 (C1orf26, Accession NM_017673). Accordingly, utilities of VGAM935 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf26. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 936 (VGAM936) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35247] VGAM936 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM936 was detected is described hereinabove with reference to Figs. 1–8.

[35248] VGAM936 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35249] VGAM936 gene encodes a VGAM936 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM936 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM936 precursor RNA is designated SEQ ID:922, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:922 is located at position 139973 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[35250] VGAM936 precursor RNA folds onto itself, forming VGAM936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35251] An enzyme complex designated DICER COMPLEX, `dices` the VGAM936 folded precursor RNA into VGAM936 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM936 RNA is designated SEQ ID:3647, and is provided hereinbelow with reference to the sequence listing part.

[35252] VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM936 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35253] VGAM936 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM936 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM936 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35254] The complementary binding of VGAM936 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM936 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM936 host target RNA into VGAM936 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35255] It is appreciated that VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM936 host target genes. The mRNA of each one of this plurality of VGAM936 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM936 RNA, herein designated VGAM RNA, and which when bound by VGAM936 RNA causes inhibition of translation of respective one or more VGAM936 host target proteins.

[35256] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM936 gene, herein designated VGAM GENE, on one or more VGAM936 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35257] It is yet further appreciated that a function of VGAM936 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM936 correlate with, and may be deduced from, the identity of the host target genes which VGAM936 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35258] Nucleotide sequences of the VGAM936 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM936 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM936 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM936 are further described hereinbelow with reference to Table 1.

[35259] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM936 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM936 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35260] As mentioned hereinabove with reference to Fig. 1, a function of VGAM936 gene, herein designated VGAM is inhibition of expression of VGAM936 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM936 correlate with, and may be deduced from, the identity of the target genes which VGAM936 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35261] DKFZp547A023 (Accession XM_052065) is a VGAM936 host target gene. DKFZp547A023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547A023, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547A023 BINDING SITE, designated SEQ ID:35943, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35262] A function of VGAM936 is therefore inhibition of DKFZp547A023 (Accession XM_052065). Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547A023. DKFZP564O123 (Accession XM_002810) is another VGAM936 host target gene. DKFZP564O123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O123 BINDING SITE, designated SEQ ID:29906, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35263] Another function of VGAM936 is therefore inhibition of DKFZP564O123 (Accession XM_002810). Accordingly,

utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O123. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM936 host target gene. ZDHHC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18490, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35264] Another function of VGAM936 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC129446 (Accession XM_072203) is another VGAM936 host target gene. LOC129446 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129446 BINDING SITE, designated SEQ ID:37468, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35265] Another function of VGAM936 is therefore inhibition of LOC129446 (Accession XM_072203). Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129446. LOC149722 (Accession XM_097709) is another VGAM936 host target gene. LOC149722 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149722 BINDING SITE, designated SEQ ID:41044, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35266] Another function of VGAM936 is therefore inhibition of LOC149722 (Accession XM_097709). Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC149722. LOC151414 (Accession XM_087197) is another VGAM936 host target gene. LOC151414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151414 BINDING SITE, designated SEQ ID:39113, to the nucleotide sequence of VGAM936 RNA, herein designated VGAM RNA, also designated SEQ ID:3647.

[35267] Another function of VGAM936 is therefore inhibition of LOC151414 (Accession XM_087197). Accordingly, utilities of VGAM936 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151414. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 937 (VGAM937) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35268] VGAM937 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM937 was detected is described hereinabove with reference to Figs. 1–8.

[35269] VGAM937 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35270] VGAM937 gene encodes a VGAM937 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM937 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM937 precursor RNA is designated SEQ ID:923, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:923 is located at position 139184 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[35271] VGAM937 precursor RNA folds onto itself, forming VGAM937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35272] An enzyme complex designated DICER COMPLEX, `dices` the VGAM937 folded precursor RNA into VGAM937 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM937 RNA is designated SEQ ID:3648, and is provided hereinbelow with reference to the sequence listing part.

[35273] VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM937 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35274] VGAM937 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM937 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM937 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35275] The complementary binding of VGAM937 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM937 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM937 host target RNA into VGAM937 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35276] It is appreciated that VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM937 host target genes. The mRNA of each one of this plurality of VGAM937 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM937 RNA, herein designated VGAM RNA, and which when bound by VGAM937 RNA causes inhibition of translation of respective one or more VGAM937 host target proteins.

[35277] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM937 gene, herein designated VGAM GENE, on one or more VGAM937 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35278] It is yet further appreciated that a function of VGAM937 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM937 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM937 correlate with, and may be deduced from, the identity of the host target genes which VGAM937 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35279] Nucleotide sequences of the VGAM937 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM937 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM937 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM937 are further described hereinbelow with reference to Table 1.

[35280] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM937 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM937 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35281] As mentioned hereinabove with reference to Fig. 1, a function of VGAM937 gene, herein designated VGAM is inhibition of expression of VGAM937 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM937 correlate with, and may be deduced from, the identity of the target genes which VGAM937 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35282] Butyrophilin, Subfamily 3, Member A3 (BTN3A3, Accession NM_006994) is a VGAM937 host target gene. BTN3A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN3A3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN3A3 BINDING SITE, designated SEQ ID:13856, to the nucleotide sequence of VGAM937 RNA, herein designated VGAM RNA, also designated SEQ ID:3648.

[35283] A function of VGAM937 is therefore inhibition of Butyrophilin, Subfamily 3, Member A3 (BTN3A3, Accession NM_006994). Accordingly, utilities of VGAM937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN3A3. FENS-1 (Accession NM_020830) is another VGAM937 host target gene. FENS-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FENS-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FENS-1 BINDING SITE, designated SEQ ID:21893, to the nucleotide sequence of VGAM937 RNA, herein designated VGAM RNA, also designated SEQ ID:3648.

[35284] Another function of VGAM937 is therefore inhibition of FENS-1 (Accession NM_020830). Accordingly, utilities of

VGAM937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FENS-1. KIAA1164 (Accession XM_045358) is another VGAM937 host target gene. KIAA1164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1164 BINDING SITE, designated SEQ ID:34440, to the nucleotide sequence of VGAM937 RNA, herein designated VGAM RNA, also designated SEQ ID:3648.

[35285] Another function of VGAM937 is therefore inhibition of KIAA1164 (Accession XM_045358). Accordingly, utilities of VGAM937 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1164. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 938 (VGAM938) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35286] VGAM938 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM938 was detected is described hereinabove with reference to Figs. 1–8.

[35287] VGAM938 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil–borne Mosaic Virus. VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35288] VGAM938 gene encodes a VGAM938 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM938 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM938 precursor RNA is designated SEQ ID:924, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:924 is located at position 709 relative to the genome of Beet Soil–borne Mosaic Virus.

[35289] VGAM938 precursor RNA folds onto itself, forming VGAM938 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35290] An enzyme complex designated DICER COMPLEX, `dices` the VGAM938 folded precursor RNA into VGAM938 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM938 RNA is designated SEQ ID:3649, and is provided hereinbelow with reference to the sequence listing part.

[35291] VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM938 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[35292] VGAM938 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM938 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM938 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35293] The complementary binding of VGAM938 RNA, herein designated VGAM RNA, to host target binding sites on VGAM938 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM938 host target RNA into VGAM938 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35294] It is appreciated that VGAM938 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM938 host target genes. The mRNA of each one of this plurality of VGAM938 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM938 RNA, herein designated VGAM RNA, and which when bound by VGAM938 RNA causes inhibition of translation of respective one or more VGAM938 host target proteins.

[35295] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM938 gene, herein designated VGAM GENE, on one or more VGAM938 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35296] It is yet further appreciated that a function of VGAM938 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM938 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM938 correlate with, and may be deduced from, the identity of the host target genes which VGAM938 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35297] Nucleotide sequences of the VGAM938 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM938 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM938 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM938 are further
described hereinbelow with reference to Table 1.

[35298] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM938 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM938 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[35299] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM938 gene, herein designated VGAM is
inhibition of expression of VGAM938 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM938 correlate with, and may be deduced
from, the identity of the target genes which VGAM938
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[35300] Protein Kinase, CAMP-dependent, Regulatory, Type II, Beta
(PRKAR2B, Accession NM_002736) is a VGAM938 host tar-

get gene. PRKAR2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAR2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR2B BINDING SITE, designated SEQ ID:8612, to the nucleotide sequence of VGAM938 RNA, herein designated VGAM RNA, also designated SEQ ID:3649.

[35301] A function of VGAM938 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type II, Beta (PRKAR2B, Accession NM_002736), a gene which type ii regulatory chains mediate membrane association by binding to anchoring proteins, including the map2 kinase. Accordingly, utilities of VGAM938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR2B. The function of PRKAR2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.LOC154789 (Accession XM_088043) is another VGAM938 host target gene. LOC154789 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by LOC154789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154789 BINDING SITE, designated SEQ ID:39486, to the nucleotide sequence of VGAM938 RNA, herein designated VGAM RNA, also designated SEQ ID:3649.

[35302] Another function of VGAM938 is therefore inhibition of LOC154789 (Accession XM_088043). Accordingly, utilities of VGAM938 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154789. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 939 (VGAM939) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35303] VGAM939 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM939 was detected is described hereinabove with reference to Figs. 1–8.

[35304] VGAM939 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35305] VGAM939 gene encodes a VGAM939 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM939 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM939 precursor RNA is designated SEQ ID:925, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:925 is located at position 1784 relative to the genome of Beet Soil-borne Mosaic Virus.

[35306] VGAM939 precursor RNA folds onto itself, forming VGAM939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35307] An enzyme complex designated DICER COMPLEX, `dices` the VGAM939 folded precursor RNA into VGAM939 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM939 RNA is designated SEQ ID:3650, and is provided hereinbelow with reference to the sequence listing part.

[35308] VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM939 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35309] VGAM939 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM939 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM939 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35310] The complementary binding of VGAM939 RNA, herein designated VGAM RNA, to host target binding sites on VGAM939 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM939 host tar–

get RNA into VGAM939 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35311] It is appreciated that VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM939 host target genes. The mRNA of each one of this plurality of VGAM939 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM939 RNA, herein designated VGAM RNA, and which when bound by VGAM939 RNA causes inhibition of translation of respective one or more VGAM939 host target proteins.

[35312] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM939 gene, herein designated VGAM GENE, on one or more VGAM939 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35313] It is yet further appreciated that a function of VGAM939 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM939 correlate with, and may be deduced from, the identity of the host target genes which VGAM939 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35314] Nucleotide sequences of the VGAM939 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM939 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM939 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM939 are further

described hereinbelow with reference to Table 1.

[35315] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM939 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM939 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35316] As mentioned hereinabove with reference to Fig. 1, a function of VGAM939 gene, herein designated VGAM is inhibition of expression of VGAM939 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM939 correlate with, and may be deduced from, the identity of the target genes which VGAM939 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35317] A Disintegrin and Metalloproteinase Domain 28 (ADAM28, Accession NM_014265) is a VGAM939 host target gene. ADAM28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ADAM28 BINDING SITE, designated SEQ ID:15540, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35318] A function of VGAM939 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 28 (ADAM28, Accession NM_014265), a gene which Member of the MDC family of metalloproteinases. Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM28. The function of ADAM28 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM608. Inducible T-cell Co-stimulator (ICOS, Accession NM_012092) is another VGAM939 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14390, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35319] Another function of VGAM939 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Tumor Necrosis Factor Receptor Superfamily, Member 1B (TNFRSF1B, Accession NM_001066) is another VGAM939 host target gene. TNFRSF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF1B BINDING SITE, designated SEQ ID:6734, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35320] Another function of VGAM939 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 1B (TNFRSF1B, Accession NM_001066), a gene which medi-

ates proinflammatory cellular responses. Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF1B. The function of TNFRSF1B has been established by previous studies. Preassembly or self-association of cytokine receptor dimers (e.g., OMIM Ref. No. 147810; IL2R, 147730; and EPOR, 133171) occurs via the same amino acid contacts that are critical for ligand binding. Chan et al. (2000) found that, in contrast, the p60 (TNFRSF1A; 191190) and p80 (TNFRSF1B) TNFA receptors self-assemble through a distinct functional domain in the TNFR extracellular domain, termed the pre-ligand assembly domain (PLAD), in the absence of ligand. Deletion of the PLAD results in monomeric presentation of p60 or p80. Flow cytometric analysis showed that efficient TNFA binding depends on receptor self-assembly. They also found that other members of the TNF receptor superfamily, including the extracellular domains of TRAIL (TNFRSF10A; 603611), CD40 (TNFRSF5; 109535), and FAS (TNFRSF6; 134637), all self-associate but do not interact with heterologous receptors. Using Jurkat T cells, which express TNFR1 but little TNFR2, and Jurkat cells stably transfected with TNFR2, Li et al. (2002) confirmed that

TNF stimulation, or stimulation with a TNFR2, but not TNFR1, agonist, causes a loss of TRAF2 (OMIM Ref. No. 601895) in the TNFR2-expressing cells, but not the parental cell line, through a ubiquitination- and proteasome-dependent process. Binding analysis indicated that TRAF2 interacts with CIAP1 (OMIM Ref. No. 601712) and CIAP2 (OMIM Ref. No. 601721), which possess E3 ubiquitin ligase (e.g. UBE3A, 601623) activity. Ubiquitination assays and SDS-PAGE analysis showed that in the presence of an E2-conjugating enzyme (e.g., UBCH7, 603721), CIAP1, but not CIAP2, induces TRAF2 ubiquitination outside of its RING domain. Both CIAPs bind but neither ubiquitinates TRAF1 (OMIM Ref. No. 601711). CIAP1 expression fails to protect TNFR2-expressing cells from TNF-induced apoptosis, whereas an E3-inactive CIAP1 mutant and wildtype CIAP2 do protect cells from TRAF2 downregulation and cause a delay in cell death. Li et al. (2002) concluded that TNFR2 stimulation causes the ubiquitination of TRAF2 by CIAP1, which can play a proapoptotic role in TNF signaling. Animal model experiments lend further support to the function of TNFRSF1B. Bruce et al. (1996) used targeted gene disruption to generate mice lacking either the p55 (TNFR1) or the p75 (TNFR2) TNF re-

ceptor; mice lacking both p55 and p75 were generated from crosses of the singly deficient mice. The TNFR-deficient (TNFR-KO) mice exhibited no overt phenotype under unchallenged conditions. Bruce et al. (1996) reported that damage to neurons caused by focal cerebral ischemia and epileptic seizures was exacerbated in the TNFR-KO mice, indicating that TNF serves a neuroprotective function. Their studies indicated that TNF protects neurons by stimulating antioxidative pathways. Injury-induced microglial activation was suppressed in TNFR-KO mice. They concluded that drugs which target TNF signaling pathways may prove beneficial in treating stroke or traumatic brain injury.

[35321] It is appreciated that the abovementioned animal model for TNFRSF1B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[35322] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35323] Chan, F. K.-M.; Chun, H. J.; Zheng, L.; Siegel, R. M.; Bui, K. L.; Lenardo, M. J. : A domain in TNF receptors that mediates ligand-independent receptor assembly and signaling.

Science 288: 2351–2354, 2000. ; and

[35324] Li, X.; Yang, Y.; Ashwell, J. D. : TNF–RII and c–IAP1 mediate ubiquitination and degradation of TRAF2. Nature 416: 345–349, 2002.

[35325] Further studies establishing the function and utilities of TNFRSF1B are found in John Hopkins OMIM database record ID 191191, and in cited publications numbered 2048, 9573, 11502–1182, 1176, 1183, 1054 and 10543 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Alpha 1,4–galactosyltransferase (A4GALT, Accession NM_017436) is another VGAM939 host target gene. A4GALT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by A4GALT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A4GALT BINDING SITE, designated SEQ ID:18894, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35326] Another function of VGAM939 is therefore inhibition of Alpha 1,4–galactosyltransferase (A4GALT, Accession

NM_017436). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A4GALT. Apg4B (Accession NM_013325) is another VGAM939 host target gene.

Apg4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Apg4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Apg4B BINDING SITE, designated SEQ ID:14974, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35327] Another function of VGAM939 is therefore inhibition of Apg4B (Accession NM_013325). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Apg4B. FLJ22405 (Accession NM_022485) is another VGAM939 host target gene. FLJ22405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ22405 BINDING SITE, designated SEQ ID:22863, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35328] Another function of VGAM939 is therefore inhibition of FLJ22405 (Accession NM_022485). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22405. HGC6.2 (Accession NM_014356) is another VGAM939 host target gene. HGC6.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGC6.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGC6.2 BINDING SITE, designated SEQ ID:15687, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35329] Another function of VGAM939 is therefore inhibition of HGC6.2 (Accession NM_014356). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGC6.2. HRD1 (Accession XM_045498) is another VGAM939 host

target gene. HRD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRD1 BINDING SITE, designated SEQ ID:34472, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35330] Another function of VGAM939 is therefore inhibition of HRD1 (Accession XM_045498). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRD1. OS4 (Accession NM_005730) is another VGAM939 host target gene. OS4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OS4 BINDING SITE, designated SEQ ID:12289, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35331] Another function of VGAM939 is therefore inhibition of OS4 (Accession NM_005730). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OS4. LOC115557 (Accession NM_133483) is another VGAM939 host target gene. LOC115557 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115557 BINDING SITE, designated SEQ ID:28556, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35332] Another function of VGAM939 is therefore inhibition of LOC115557 (Accession NM_133483). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115557. LOC124976 (Accession XM_058879) is another VGAM939 host target gene. LOC124976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124976, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124976 BINDING SITE, designated SEQ ID:36781, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35333] Another function of VGAM939 is therefore inhibition of LOC124976 (Accession XM_058879). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124976. LOC148343 (Accession XM_086150) is another VGAM939 host target gene. LOC148343 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148343 BINDING SITE, designated SEQ ID:38521, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35334] Another function of VGAM939 is therefore inhibition of LOC148343 (Accession XM_086150). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC148343. LOC150175 (Accession XM_086806) is another VGAM939 host target gene. LOC150175 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150175 BINDING SITE, designated SEQ ID:38883, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35335] Another function of VGAM939 is therefore inhibition of LOC150175 (Accession XM_086806). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150175. LOC150215 (Accession XM_086813) is another VGAM939 host target gene. LOC150215 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150215 BINDING SITE, designated SEQ ID:38887, to the nucleotide sequence of VGAM939 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3650.

[35336] Another function of VGAM939 is therefore inhibition of LOC150215 (Accession XM_086813). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150215. LOC150218 (Accession XM_086850) is another VGAM939 host target gene. LOC150218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150218 BINDING SITE, designated SEQ ID:38914, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35337] Another function of VGAM939 is therefore inhibition of LOC150218 (Accession XM_086850). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150218. LOC152002 (Accession XM_087360) is another VGAM939 host target gene. LOC152002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152002, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152002 BINDING SITE, designated SEQ ID:39195, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35338] Another function of VGAM939 is therefore inhibition of LOC152002 (Accession XM_087360). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152002. LOC152765 (Accession XM_087519) is another VGAM939 host target gene. LOC152765 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152765 BINDING SITE, designated SEQ ID:39312, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35339] Another function of VGAM939 is therefore inhibition of LOC152765 (Accession XM_087519). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC152765. LOC166979 (Accession XM_094210) is another VGAM939 host target gene. LOC166979 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC166979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166979 BINDING SITE, designated SEQ ID:40225, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35340] Another function of VGAM939 is therefore inhibition of LOC166979 (Accession XM_094210). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166979. LOC196746 (Accession XM_113595) is another VGAM939 host target gene. LOC196746 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196746 BINDING SITE, designated SEQ ID:42289, to

the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35341] Another function of VGAM939 is therefore inhibition of LOC196746 (Accession XM_113595). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196746. LOC253962 (Accession XM_172968) is another VGAM939 host target gene. LOC253962 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253962 BINDING SITE, designated SEQ ID:46224, to the nucleotide sequence of VGAM939 RNA, herein designated VGAM RNA, also designated SEQ ID:3650.

[35342] Another function of VGAM939 is therefore inhibition of LOC253962 (Accession XM_172968). Accordingly, utilities of VGAM939 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253962. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 940 (VGAM940) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35343] VGAM940 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM940 was detected is described hereinabove with reference to Figs. 1–8.

[35344] VGAM940 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35345] VGAM940 gene encodes a VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM940 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM940 precursor RNA is designated SEQ ID:926, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:926 is located at position 2221 relative to the genome of Beet Soil-borne Mosaic Virus.

[35346] VGAM940 precursor RNA folds onto itself, forming VGAM940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35347] An enzyme complex designated DICER COMPLEX, `dices` the VGAM940 folded precursor RNA into VGAM940 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM940 RNA is designated SEQ ID:3651, and is provided hereinbelow with reference to the sequence listing part.

[35348] VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM940 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM940 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35349] VGAM940 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM940 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM940 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35350] The complementary binding of VGAM940 RNA, herein designated VGAM RNA, to host target binding sites on VGAM940 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM940 host target RNA into VGAM940 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35351] It is appreciated that VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM940 host target genes. The mRNA of each one of this plurality of VGAM940 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM940 RNA, herein designated VGAM RNA, and which when bound by VGAM940 RNA causes inhibition of translation of respective one or more VGAM940 host target proteins.

[35352] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM940 gene, herein designated VGAM GENE, on one or more VGAM940 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35353] It is yet further appreciated that a function of VGAM940 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM940 correlate with, and may be deduced from, the

identity of the host target genes which VGAM940 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35354] Nucleotide sequences of the VGAM940 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM940 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM940 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM940 are further described hereinbelow with reference to Table 1.

[35355] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM940 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM940 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35356] As mentioned hereinabove with reference to Fig. 1, a function of VGAM940 gene, herein designated VGAM is inhibition of expression of VGAM940 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM940 correlate with, and may be deduced from, the identity of the target genes which VGAM940

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35357] B-cell CLL/lymphoma 2 (BCL2, Accession NM_000633) is a VGAM940 host target gene. BCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2 BINDING SITE, designated SEQ ID:6257, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35358] A function of VGAM940 is therefore inhibition of B-cell CLL/lymphoma 2 (BCL2, Accession NM_000633). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2. CAMP Responsive Element Binding Protein-like 2 (CREBL2, Accession NM_001310) is another VGAM940 host target gene. CREBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CREBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREBL2 BINDING SITE, designated SEQ ID:6258, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

tarity of the nucleotide sequences of CREBL2 BINDING SITE, designated SEQ ID:6992, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35359] Another function of VGAM940 is therefore inhibition of CAMP Responsive Element Binding Protein-like 2 (CREBL2, Accession NM_001310). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREBL2. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_004007) is another VGAM940 host target gene. DMD BINDING SITE1 and DMD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 and DMD BINDING SITE2, designated SEQ ID:10162 and SEQ ID:10176 respectively, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35360] Another function of VGAM940 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker

types) (DMD, Accession NM_004007), a gene which muscular dystrophy . Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218. Myotubularin Related Protein 8 (MTMR8, Accession NM_015458) is another VGAM940 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17740, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35361] Another function of VGAM940 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Tec Protein Tyrosine Kinase (TEC, Accession NM_003215) is another VGAM940 host target gene. TEC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEC BINDING SITE, designated SEQ ID:9215, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35362] Another function of VGAM940 is therefore inhibition of Tec Protein Tyrosine Kinase (TEC, Accession NM_003215). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEC. Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM_001243) is another VGAM940 host target gene. TNFRSF8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TNFRSF8, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF8 BINDING SITE, designated SEQ ID:6907, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35363] Another function of VGAM940 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM_001243), a gene which regulates gene expression through activation of nf-kappab. Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF8. The function of TNFRSF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM154. Zinc Finger Protein (C2H2 type) 277 (ZNF277, Accession NM_021994) is another VGAM940 host target gene. ZNF277 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF277

BINDING SITE, designated SEQ ID:22534, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35364] Another function of VGAM940 is therefore inhibition of Zinc Finger Protein (C2H2 type) 277 (ZNF277, Accession NM_021994). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF277. FHX (Accession NM_018416) is another VGAM940 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20456, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35365] Another function of VGAM940 is therefore inhibition of FHX (Accession NM_018416). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHX. FLJ10035 (Accession NM_017974) is another VGAM940 host target gene. FLJ10035 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ10035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10035 BINDING SITE, designated SEQ ID:19705, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35366] Another function of VGAM940 is therefore inhibition of FLJ10035 (Accession NM_017974). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10035. FLJ10283 (Accession NM_018046) is another VGAM940 host target gene. FLJ10283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10283 BINDING SITE, designated SEQ ID:19794, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35367] Another function of VGAM940 is therefore inhibition of

FLJ10283 (Accession NM_018046). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10283. FLJ20127 (Accession NM_017678) is another VGAM940 host target gene. FLJ20127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20127 BINDING SITE, designated SEQ ID:19219, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35368] Another function of VGAM940 is therefore inhibition of FLJ20127 (Accession NM_017678). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20127. KIAA0828 (Accession XM_088105) is another VGAM940 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39514, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35369] Another function of VGAM940 is therefore inhibition of KIAA0828 (Accession XM_088105). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. KIAA1163 (Accession XM_086231) is another VGAM940 host target gene. KIAA1163 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1163 BINDING SITE, designated SEQ ID:38560, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35370] Another function of VGAM940 is therefore inhibition of KIAA1163 (Accession XM_086231). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1163. KIAA1434 (Accession XM_045585) is another

VGAM940 host target gene. KIAA1434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1434 BINDING SITE, designated SEQ ID:34487, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35371] Another function of VGAM940 is therefore inhibition of KIAA1434 (Accession XM_045585). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1434. KIAA1821 (Accession XM_050101) is another VGAM940 host target gene. KIAA1821 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1821 BINDING SITE, designated SEQ ID:35553, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35372] Another function of VGAM940 is therefore inhibition of KIAA1821 (Accession XM_050101). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1821. Macrophage Erythroblast Attacher (MAEA, Accession NM_005882) is another VGAM940 host target gene. MAEA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAEA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAEA BINDING SITE, designated SEQ ID:12494, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35373] Another function of VGAM940 is therefore inhibition of Macrophage Erythroblast Attacher (MAEA, Accession NM_005882). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAEA. Zinc Finger Protein 31 (KOX 29) (ZNF31, Accession XM_036305) is another VGAM940 host target gene. ZNF31 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF31, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF31 BINDING SITE, designated SEQ ID:32422, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35374] Another function of VGAM940 is therefore inhibition of Zinc Finger Protein 31 (KOX 29) (ZNF31, Accession XM_036305). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF31. LOC118709 (Accession XM_058338) is another VGAM940 host target gene. LOC118709 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC118709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118709 BINDING SITE, designated SEQ ID:36599, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35375] Another function of VGAM940 is therefore inhibition of LOC118709 (Accession XM_058338). Accordingly, utilities

of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118709. LOC158310 (Accession XM_098919) is another VGAM940 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41946, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35376] Another function of VGAM940 is therefore inhibition of LOC158310 (Accession XM_098919). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. LOC256519 (Accession XM_171056) is another VGAM940 host target gene. LOC256519 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC256519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256519 BINDING SITE, designated SEQ ID:45852, to the nucleotide sequence of VGAM940 RNA, herein designated VGAM RNA, also designated SEQ ID:3651.

[35377] Another function of VGAM940 is therefore inhibition of LOC256519 (Accession XM_171056). Accordingly, utilities of VGAM940 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256519. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 941 (VGAM941) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35378] VGAM941 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM941 was detected is described hereinabove with reference to Figs. 1–8.

[35379] VGAM941 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35380] VGAM941 gene encodes a VGAM941 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM941 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM941 precursor RNA is designated SEQ ID:927, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:927 is located at position 5149 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[35381] VGAM941 precursor RNA folds onto itself, forming VGAM941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35382] An enzyme complex designated DICER COMPLEX, `dices` the VGAM941 folded precursor RNA into VGAM941 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM941 RNA is designated SEQ ID:3652, and is provided hereinbelow with reference to the sequence listing part.

[35383] VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM941 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35384] VGAM941 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM941 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM941 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35385] The complementary binding of VGAM941 RNA, herein designated VGAM RNA, to host target binding sites on VGAM941 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM941 host target RNA into VGAM941 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35386] It is appreciated that VGAM941 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM941 host target genes. The mRNA of each one of this plurality of VGAM941 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM941 RNA, herein designated VGAM RNA, and which when bound by VGAM941 RNA causes inhibition of translation of respective one or more VGAM941 host target proteins.

[35387] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM941 gene, herein designated VGAM GENE, on one or more VGAM941 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[35388] It is yet further appreciated that a function of VGAM941 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM941 correlate with, and may be deduced from, the identity of the host target genes which VGAM941 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35389] Nucleotide sequences of the VGAM941 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM941 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM941 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM941 are further described hereinbelow with reference to Table 1.

[35390] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM941 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM941 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35391] As mentioned hereinabove with reference to Fig. 1, a function of VGAM941 gene, herein designated VGAM is inhibition of expression of VGAM941 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM941 correlate with, and may be deduced from, the identity of the target genes which VGAM941 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35392] Ataxia Telangiectasia Mutated (includes complementation groups A, C and D) (ATM, Accession NM_138292) is a VGAM941 host target gene. ATM BINDING SITE1 and ATM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATM BINDING SITE1 and ATM BINDING SITE2, designated SEQ ID:28704 and SEQ ID:28706 respectively, to the nucleotide sequence of VGAM941 RNA, herein designated

VGAM RNA, also designated SEQ ID:3652.

[35393] A function of VGAM941 is therefore inhibition of Ataxia Telangiectasia Mutated (includes complementation groups A, C and D) (ATM, Accession NM_138292). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATM. Fc Fragment of IgG, Low Affinity Ila, Receptor For (CD32) (FCGR2A, Accession XM_086483) is another VGAM941 host target gene. FCGR2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCGR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCGR2A BINDING SITE, designated SEQ ID:38698, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35394] Another function of VGAM941 is therefore inhibition of Fc Fragment of IgG, Low Affinity Ila, Receptor For (CD32) (FCGR2A, Accession XM_086483), a gene which binds IgG immune complexes; member of the immunoglobulin superfamily. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with FCGR2A. The function of FCGR2A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444.Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293) is another VGAM941 host target gene. LAMC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMC1 BINDING SITE, designated SEQ ID:8074, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35395] Another function of VGAM941 is therefore inhibition of Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293), a gene which may mediate the attachment, migration, and organization of cells into tissues. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMC1. The function of LAMC1 and its association with various diseases and clinical conditions, has

been established by previous studies, as described hereinabove with reference to VGAM812. Myosin X (MYO10, Accession NM_012334) is another VGAM941 host target gene. MYO10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO10 BINDING SITE, designated SEQ ID:14731, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35396] Another function of VGAM941 is therefore inhibition of Myosin X (MYO10, Accession NM_012334), a gene which is an unconventional myosin. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO10. The function of MYO10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. NADH Dehydrogenase (ubiquinone) Flavoprotein 3, 10kDa (NDUFV3, Accession NM_021075) is another VGAM941 host target gene. NDUFV3 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NDUFV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDUFV3 BINDING SITE, designated SEQ ID:22043, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35397] Another function of VGAM941 is therefore inhibition of NADH Dehydrogenase (ubiquinone) Flavoprotein 3, 10kDa (NDUFV3, Accession NM_021075), a gene which transports electrons from NADH to ubiquinone. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDUFV3. The function of NDUFV3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM626. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is another VGAM941 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12881, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35398] Another function of VGAM941 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117. Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749) is another VGAM941 host target gene. SLC20A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC20A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of SLC20A2 BINDING SITE, designated SEQ ID:13599, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35399] Another function of VGAM941 is therefore inhibition of Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749), a gene which is a sodium-phosphate symporter. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC20A2. The function of SLC20A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_000458) is another VGAM941 host target gene. TCF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE, designated SEQ ID:6074, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA,

also designated SEQ ID:3652.

[35400] Another function of VGAM941 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_000458), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118. Basic Leucine Zipper Nuclear Factor 1 (JEM-1) (BLZF1, Accession NM_003666) is another VGAM941 host target gene. BLZF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLZF1 BINDING SITE, designated SEQ ID:9747, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35401] Another function of VGAM941 is therefore inhibition of Basic Leucine Zipper Nuclear Factor 1 (JEM-1) (BLZF1, Ac-

cession NM_003666). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLZF1. Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM_002384) is another VGAM941 host target gene. DGKD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKD BINDING SITE, designated SEQ ID:29877, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35402] Another function of VGAM941 is therefore inhibition of Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM_002384). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKD. FLJ21195 (Accession NM_022469) is another VGAM941 host target gene. FLJ21195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21195 BINDING SITE, designated SEQ ID:22824, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35403] Another function of VGAM941 is therefore inhibition of FLJ21195 (Accession NM_022469). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21195. KIAA0164 (Accession NM_014739) is another VGAM941 host target gene. KIAA0164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0164 BINDING SITE, designated SEQ ID:16404, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35404] Another function of VGAM941 is therefore inhibition of KIAA0164 (Accession NM_014739). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0164. KIAA0350 (Accession XM_028332) is another VGAM941 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30661, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35405] Another function of VGAM941 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA1396 (Accession XM_032054) is another VGAM941 host target gene. KIAA1396 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1396, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1396 BINDING SITE, designated SEQ ID:31546, to the nucleotide sequence of VGAM941 RNA, herein designated

VGAM RNA, also designated SEQ ID:3652.

[35406] Another function of VGAM941 is therefore inhibition of KIAA1396 (Accession XM_032054). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1396. KIAA1853 (Accession XM_045184) is another VGAM941 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34382, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35407] Another function of VGAM941 is therefore inhibition of KIAA1853 (Accession XM_045184). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1853. KIAA1884 (Accession XM_055539) is another VGAM941 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1884, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36291, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35408] Another function of VGAM941 is therefore inhibition of KIAA1884 (Accession XM_055539). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM_031469) is another VGAM941 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25526, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35409] Another function of VGAM941 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2

(SH3BGRL2, Accession NM_031469). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL2. LOC127255 (Accession NM_145258) is another VGAM941 host target gene. LOC127255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127255 BINDING SITE, designated SEQ ID:29773, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35410] Another function of VGAM941 is therefore inhibition of LOC127255 (Accession NM_145258). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127255. LOC158563 (Accession XM_088606) is another VGAM941 host target gene. LOC158563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158563 BINDING SITE, designated SEQ ID:39868, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35411] Another function of VGAM941 is therefore inhibition of LOC158563 (Accession XM_088606). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158563. LOC163081 (Accession XM_091987) is another VGAM941 host target gene. LOC163081 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163081 BINDING SITE, designated SEQ ID:40085, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35412] Another function of VGAM941 is therefore inhibition of LOC163081 (Accession XM_091987). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163081. LOC51279 (Accession NM_016546) is an-

other VGAM941 host target gene. LOC51279 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51279 BINDING SITE, designated SEQ ID:18616, to the nucleotide sequence of VGAM941 RNA, herein designated VGAM RNA, also designated SEQ ID:3652.

[35413] Another function of VGAM941 is therefore inhibition of LOC51279 (Accession NM_016546). Accordingly, utilities of VGAM941 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51279. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 942 (VGAM942) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35414] VGAM942 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM942 was detected is described

hereinabove with reference to Figs. 1–8.

[35415] VGAM942 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and Kidney Necrosis Virus. VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35416] VGAM942 gene encodes a VGAM942 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM942 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM942 precursor RNA is designated SEQ ID:928, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:928 is located at position 3787 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[35417] VGAM942 precursor RNA folds onto itself, forming VGAM942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35418] An enzyme complex designated DICER COMPLEX, `dices` the VGAM942 folded precursor RNA into VGAM942 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM942 RNA is designated SEQ ID:3653, and is provided hereinbelow with reference to the sequence listing part.

[35419] VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM942 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35420] VGAM942 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM942 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM942 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM942 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35421] The complementary binding of VGAM942 RNA, herein designated VGAM RNA, to host target binding sites on VGAM942 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM942 host target RNA into VGAM942 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35422] It is appreciated that VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM942 host target genes. The mRNA of each one of this plurality of VGAM942 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM942 RNA, herein designated VGAM RNA, and which when bound by VGAM942 RNA causes inhibition of translation of respective one or more VGAM942 host target proteins.

[35423] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM942 gene, herein designated VGAM GENE, on one or more VGAM942 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35424] It is yet further appreciated that a function of VGAM942 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM942 correlate with, and may be deduced from, the identity of the host target genes which VGAM942 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35425] Nucleotide sequences of the VGAM942 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM942 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM942 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM942 are further described hereinbelow with reference to Table 1.

[35426] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM942 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM942 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35427] As mentioned hereinabove with reference to Fig. 1, a function of VGAM942 gene, herein designated VGAM is inhibition of expression of VGAM942 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM942 correlate with, and may be deduced from, the identity of the target genes which VGAM942 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35428] EphB2 (EPHB2, Accession NM_004442) is a VGAM942 host target gene. EPHB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of EPHB2 BINDING SITE, designated SEQ ID:10732, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35429] A function of VGAM942 is therefore inhibition of EphB2 (EPHB2, Accession NM_004442), a gene which Eph-related receptor tyrosine kinase B2; may have a role in neurogenesis. Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB2. The function of EPHB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM533. GATA Binding Protein 2 (GATA2, Accession NM_002050) is another VGAM942 host target gene. GATA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE, designated SEQ ID:7804, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA,

also designated SEQ ID:3653.

[35430] Another function of VGAM942 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM_002050). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. GRAF (Accession NM_015071) is another VGAM942 host target gene. GRAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRAF BINDING SITE, designated SEQ ID:17441, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35431] Another function of VGAM942 is therefore inhibition of GRAF (Accession NM_015071), a gene which is a GTPase activating protein for p21-rac. Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRAF. The function of GRAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM430. Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM_001569) is another VGAM942 host target gene. IRAK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRAK1 BINDING SITE, designated SEQ ID:7298, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35432] Another function of VGAM942 is therefore inhibition of Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM_001569). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK1. KIAA0450 (Accession NM_014638) is another VGAM942 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated

SEQ ID:16027, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35433] Another function of VGAM942 is therefore inhibition of KIAA0450 (Accession NM_014638). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA0789 (Accession XM_033113) is another VGAM942 host target gene. KIAA0789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0789 BINDING SITE, designated SEQ ID:31845, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35434] Another function of VGAM942 is therefore inhibition of KIAA0789 (Accession XM_033113). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0789. LIG-1 (Accession XM_033712) is another VGAM942 host target gene. LIG-1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by LIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIG-1 BINDING SITE, designated SEQ ID:31950, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35435] Another function of VGAM942 is therefore inhibition of LIG-1 (Accession XM_033712). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG-1. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM_024607) is another VGAM942 host target gene. PPP1R3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3B BINDING SITE, designated SEQ ID:23855, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35436] Another function of VGAM942 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM_024607). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3B. STI2 (Accession XM_114335) is another VGAM942 host target gene. STI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STI2 BINDING SITE, designated SEQ ID:42876, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35437] Another function of VGAM942 is therefore inhibition of STI2 (Accession XM_114335). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STI2. LOC51285 (Accession NM_016563) is another VGAM942 host target gene. LOC51285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51285, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51285 BINDING SITE, designated SEQ ID:18637, to the nucleotide sequence of VGAM942 RNA, herein designated VGAM RNA, also designated SEQ ID:3653.

[35438] Another function of VGAM942 is therefore inhibition of LOC51285 (Accession NM_016563). Accordingly, utilities of VGAM942 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51285. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 943 (VGAM943) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35439] VGAM943 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM943 was detected is described hereinabove with reference to Figs. 1–8.

[35440] VGAM943 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Spleen and

Kidney Necrosis Virus. VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35441] VGAM943 gene encodes a VGAM943 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM943 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM943 precursor RNA is designated SEQ ID:929, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:929 is located at position 6007 relative to the genome of Infectious Spleen and Kidney Necrosis Virus.

[35442] VGAM943 precursor RNA folds onto itself, forming VGAM943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35443] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM943 folded precursor RNA into VGAM943 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM943 RNA is designated SEQ ID:3654, and is provided hereinbelow with reference to the sequence listing part.

[35444] VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM943 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35445] VGAM943 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM943 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM943 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35446] The complementary binding of VGAM943 RNA, herein designated VGAM RNA, to host target binding sites on VGAM943 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM943 host target RNA into VGAM943 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35447] It is appreciated that VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM943 host target genes. The mRNA of each one of this plurality of VGAM943 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM943 RNA, herein designated VGAM RNA, and which when bound by VGAM943 RNA causes inhibition of translation of respective one or more VGAM943 host target proteins.

[35448] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM943 gene, herein designated VGAM GENE, on one or more VGAM943 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35449] It is yet further appreciated that a function of VGAM943 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGAM943 correlate with, and may be deduced from, the identity of the host target genes which VGAM943 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35450] Nucleotide sequences of the VGAM943 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM943 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM943 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM943 are further described hereinbelow with reference to Table 1.

- [35451] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM943 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM943 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [35452] As mentioned hereinabove with reference to Fig. 1, a function of VGAM943 gene, herein designated VGAM is inhibition of expression of VGAM943 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM943 correlate with, and may be deduced from, the identity of the target genes which VGAM943 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [35453] Adenomatosis Polyposis Coli (APC, Accession NM_000038) is a VGAM943 host target gene. APC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APC BINDING SITE, designated SEQ ID:5482, to the nucleotide sequence of

VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35454] A function of VGAM943 is therefore inhibition of Adenomatosis Polyposis Coli (APC, Accession NM_000038). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APC. Cadherin 17, LI Cadherin (liver-intestine) (CDH17, Accession NM_004063) is another VGAM943 host target gene. CDH17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH17 BINDING SITE, designated SEQ ID:10268, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35455] Another function of VGAM943 is therefore inhibition of Cadherin 17, LI Cadherin (liver-intestine) (CDH17, Accession NM_004063), a gene which may have a role in the morphological organization of liver and intestine and involved in intestinal peptide transport. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CDH17. The function of CDH17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729) is another VGAM943 host target gene. DIAPH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIAPH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIAPH2 BINDING SITE, designated SEQ ID:13558, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35456] Another function of VGAM943 is therefore inhibition of Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729), a gene which may affect in oogenesis. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIAPH2. The function of DIAPH2 and its association with various diseases and clinical conditions, has been established by previous studies, as described here-

in above with reference to VGAM129. Glucosaminyl (N-acetyl) Transferase 2, I-branching Enzyme (GCNT2, Accession NM_001491) is another VGAM943 host target gene. GCNT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GCNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCNT2 BINDING SITE, designated SEQ ID:7240, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35457] Another function of VGAM943 is therefore inhibition of Glucosaminyl (N-acetyl) Transferase 2, I-branching Enzyme (GCNT2, Accession NM_001491), a gene which converts linear into branched poly-N-acetyllactosaminoglycans. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCNT2. The function of GCNT2 has been established by previous studies. The blood group i/I antigens were the first identified alloantigens that display a dramatic change during human development (OMIM Ref. No. 110800). The i and I

antigens are determined by linear and branched poly-N-acetyllactosaminoglycans, respectively. In human erythrocytes during embryonic development, the fetal (i) antigen is replaced by the adult (I) antigen as the result of the appearance of a beta-

1,6-N-acetylglucosaminyltransferase, the I-branching enzyme (GCNT2). Bierhuizen et al. (1993) cloned the cDNA for the branching enzyme that converts the linear form into the branched form and studied its expression with development of I antigen in transfected cells. The cDNA sequence predicted a protein of type II membrane topology as has been found for all other mammalian glycosyltransferases. Comparison of the amino acid sequence with those of other glycosyltransferases revealed that this I-branching enzyme and another beta-

1,6,N-acetylglucosaminyltransferase that forms a branch in O-glycans (GCNT1; 600391) are strongly homologous in the center of their putative catalytic domains.

[35458] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35459] Bierhuizen, M. F. A.; Mattei, M.-G.; Fukuda, M. : Expression of the developmental I antigen by a cloned human

cDNA encoding a member of a beta-1,6-N-acetylglucosaminyltransferase gene family. Genes Dev. 7: 468-478, 1993. ; and

[35460] Lin-Chu, M.; Broadberry, R. E.; Okubo, Y.; Tanaka, M. : The i phenotype and congenital cataracts among Chinese in Taiwan (Letter) Transfusion 31: 676-677, 1991.

[35461] Further studies establishing the function and utilities of GCNT2 are found in John Hopkins OMIM database record ID 600429, and in cited publications numbered 12154-12156, 4585, 758 and 12157-12158 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Histidine Ammonia-lyase (HAL, Accession NM_002108) is another VGAM943 host target gene. HAL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HAL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAL BINDING SITE, designated SEQ ID:7887, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35462] Another function of VGAM943 is therefore inhibition of Histidine Ammonia-lyase (HAL, Accession NM_002108).

Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAL. Sterol Carrier Protein 2 (SCP2, Accession NM_002979) is another VGAM943 host target gene. SCP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCP2 BINDING SITE, designated SEQ ID:8881, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35463] Another function of VGAM943 is therefore inhibition of Sterol Carrier Protein 2 (SCP2, Accession NM_002979), a gene which may regulate steroidogenesis. Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCP2. The function of SCP2 has been established by previous studies. During meiotic prophase, chromosomes are arranged along proteinaceous axes called axial elements. In rat, the major protein components of axial elements are proteins of 30, 33, and 190 kD. The 30- and 33-kD proteins are closely related and appear to be prod-

ucts of a single gene, Scp3 (synaptonemal complex protein-3; 604759). Offenberger et al. (1998) isolated rat testis cDNAs encoding the 190-kD protein, which they designated Scp2. Sequence analysis revealed that Scp2 is a basic protein, with a pI of 8. Scp2 contains 2 clusters of S/T-P motifs, which are common in DNA-binding proteins, and a C-terminal coiled-coil region. In Southwestern blot experiments, recombinant Scp2 bound DNA. Using immunocytochemistry, Offenberger et al. (1998) determined that Scp2 localizes specifically to the synaptonemal complex in the nuclei of rat testis meiotic prophase nuclei. Northern blot analysis indicated that Scp2 is expressed exclusively in testis. The authors noted that Scp2 shows some similarity at the amino acid sequence and secondary structural level to the *S. cerevisiae* Red1 protein, which is involved in meiotic recombination and the assembly of axial elements of synaptonemal complexes. They speculated that Scp2 is a DNA-binding protein involved in the structural organization of meiotic prophase chromosomes. By screening a human testis library with a partial rat Scp2 cDNA, Schalk et al. (1999) isolated cDNAs encoding human SCP2. The predicted 1,530-amino acid human protein shares 63% amino acid identity with rat Scp2. Like rat Scp2, human

SCP2 contains S/T-P motifs, 2 nuclear targeting signals, and a C-terminal coiled-coil region.

[35464] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35465] Offenberg, H. H.; Schalk, J. A. C.; Meuwissen, R. L. J.; van Aalderen, M.; Kester, H. A.; Dietrich, A. J. J.; Heyting, C. : SCP2: a major protein component of the axial elements of synaptonemal complexes of the rat. *Nucleic Acids Res.* 26: 2572-2579, 1998. ; and

[35466] Schalk, J. A. C.; Offenberg, H. H.; Peters, E.; Groot, N. P. B.; Hoovers, J. M. N.; Heyting, C. : Isolation and characterization of the human SCP2 cDNA and chromosomal localization of t.

[35467] Further studies establishing the function and utilities of SCP2 are found in John Hopkins OMIM database record ID 604105, and in cited publications numbered 7057-7058 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ10759 (Accession NM_018207) is another VGAM943 host target gene. FLJ10759 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10759, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10759 BINDING SITE, designated SEQ ID:20103, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35468] Another function of VGAM943 is therefore inhibition of FLJ10759 (Accession NM_018207). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10759. FLJ20151 (Accession NM_017689) is another VGAM943 host target gene. FLJ20151 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20151, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20151 BINDING SITE, designated SEQ ID:19246, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35469] Another function of VGAM943 is therefore inhibition of FLJ20151 (Accession NM_017689). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ20151. FLJ21617 (Accession NM_030897) is another VGAM943 host target gene. FLJ21617 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ21617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21617 BINDING SITE, designated SEQ ID:25166, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35470] Another function of VGAM943 is therefore inhibition of FLJ21617 (Accession NM_030897). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21617. KIAA0673 (Accession XM_030915) is another VGAM943 host target gene. KIAA0673 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0673 BINDING SITE, designated SEQ ID:31214, to the nucleotide sequence of

VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35471] Another function of VGAM943 is therefore inhibition of KIAA0673 (Accession XM_030915). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0673. KLK15 (Accession NM_138563) is another VGAM943 host target gene. KLK15 BINDING SITE1 and KLK15 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK15, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK15 BINDING SITE1 and KLK15 BINDING SITE2, designated SEQ ID:28861 and SEQ ID:23263 respectively, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35472] Another function of VGAM943 is therefore inhibition of KLK15 (Accession NM_138563). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK15. Syndecan 3 (N-syndecan) (SDC3, Accession NM_014654)

is another VGAM943 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16084, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35473] Another function of VGAM943 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM_014654). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215) is another VGAM943 host target gene. TGOLN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TGOLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGOLN2 BINDING SITE, designated SEQ ID:32021, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3654.

[35474] Another function of VGAM943 is therefore inhibition of Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGOLN2. LOC125268 (Accession XM_071960) is another VGAM943 host target gene. LOC125268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC125268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125268 BINDING SITE, designated SEQ ID:37453, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35475] Another function of VGAM943 is therefore inhibition of LOC125268 (Accession XM_071960). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125268. LOC144017 (Accession XM_096520) is another VGAM943 host target gene. LOC144017 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC144017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144017 BINDING SITE, designated SEQ ID:40388, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35476] Another function of VGAM943 is therefore inhibition of LOC144017 (Accession XM_096520). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144017. LOC148137 (Accession NM_144692) is another VGAM943 host target gene. LOC148137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148137 BINDING SITE, designated SEQ ID:29513, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35477] Another function of VGAM943 is therefore inhibition of LOC148137 (Accession NM_144692). Accordingly, utilities

of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148137. LOC204970 (Accession XM_114795) is another VGAM943 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43073, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35478] Another function of VGAM943 is therefore inhibition of LOC204970 (Accession XM_114795). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC219654 (Accession XM_166095) is another VGAM943 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC219654 BINDING SITE, designated SEQ ID:43878, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35479] Another function of VGAM943 is therefore inhibition of LOC219654 (Accession XM_166095). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC253539 (Accession XM_171134) is another VGAM943 host target gene. LOC253539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253539 BINDING SITE, designated SEQ ID:45938, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35480] Another function of VGAM943 is therefore inhibition of LOC253539 (Accession XM_171134). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253539. LOC254559 (Accession XM_172931) is another VGAM943 host target gene. LOC254559 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254559 BINDING SITE, designated SEQ ID:46197, to the nucleotide sequence of VGAM943 RNA, herein designated VGAM RNA, also designated SEQ ID:3654.

[35481] Another function of VGAM943 is therefore inhibition of LOC254559 (Accession XM_172931). Accordingly, utilities of VGAM943 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254559. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 944 (VGAM944) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35482] VGAM944 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM944 was detected is described hereinabove with reference to Figs. 1-8.

[35483] VGAM944 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 7. VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35484] VGAM944 gene encodes a VGAM944 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM944 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM944 precursor RNA is designated SEQ ID:930, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:930 is located at position 97457 relative to the genome of Human Herpesvirus 7.

[35485] VGAM944 precursor RNA folds onto itself, forming VGAM944 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[35486] An enzyme complex designated DICER COMPLEX, `dices` the VGAM944 folded precursor RNA into VGAM944 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM944 RNA is designated SEQ ID:3655, and is provided hereinbelow with reference to the sequence listing part.

[35487] VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM944 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35488] VGAM944 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM944 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM944 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM944 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35489] The complementary binding of VGAM944 RNA, herein designated VGAM RNA, to host target binding sites on VGAM944 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM944 host target RNA into VGAM944 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35490] It is appreciated that VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM944 host target genes. The mRNA of each one of this plurality of VGAM944 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM944 RNA, herein designated VGAM RNA, and which when bound by VGAM944 RNA causes inhibition of translation of respective one or more VGAM944 host target proteins.

[35491] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM944 gene, herein designated VGAM GENE, on one or more VGAM944 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35492] It is yet further appreciated that a function of VGAM944 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM944 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM944 correlate with, and may be deduced from, the identity of the host target genes which VGAM944 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35493] Nucleotide sequences of the VGAM944 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM944 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM944 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM944 are further described hereinbelow with reference to Table 1.

[35494] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM944 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM944 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35495] As mentioned hereinabove with reference to Fig. 1, a function of VGAM944 gene, herein designated VGAM is inhibition of expression of VGAM944 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM944 correlate with, and may be deduced from, the identity of the target genes which VGAM944 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35496] PRO1386 (Accession NM_031269) is a VGAM944 host target gene. PRO1386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of PRO1386 BINDING SITE, designated SEQ ID:25289, to the nucleotide sequence of VGAM944 RNA, herein designated VGAM RNA, also designated SEQ ID:3655.

[35497] A function of VGAM944 is therefore inhibition of PRO1386 (Accession NM_031269). Accordingly, utilities of VGAM944 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1386. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 945 (VGAM945) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35498] VGAM945 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM945 was detected is described hereinabove with reference to Figs. 1–8.

[35499] VGAM945 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 7. VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35500] VGAM945 gene encodes a VGAM945 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM945 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM945 precursor RNA is designated SEQ ID:931, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:931 is located at position 98645 relative to the genome of Human Herpesvirus 7.

[35501] VGAM945 precursor RNA folds onto itself, forming VGAM945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35502] An enzyme complex designated DICER COMPLEX, `dices` the VGAM945 folded precursor RNA into VGAM945 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM945 RNA is designated SEQ ID:3656, and is provided hereinbelow with reference to the sequence listing part.

[35503] VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM945 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35504] VGAM945 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM945 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM945 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[35505] The complementary binding of VGAM945 RNA, herein designated VGAM RNA, to host target binding sites on VGAM945 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM945 host target RNA into VGAM945 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35506] It is appreciated that VGAM945 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM945 host target genes. The mRNA of each one of this plurality of VGAM945 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM945 RNA, herein designated VGAM RNA, and which when bound by VGAM945 RNA causes inhibition of translation of respective one or more VGAM945 host target proteins.

[35507] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM945 gene, herein designated VGAM GENE, on one or more VGAM945 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[35508] It is yet further appreciated that a function of VGAM945 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM945 correlate with, and may be deduced from, the identity of the host target genes which VGAM945 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35509] Nucleotide sequences of the VGAM945 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM945 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM945 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM945 are further described hereinbelow with reference to Table 1.

[35510] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM945 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM945 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35511] As mentioned hereinabove with reference to Fig. 1, a function of VGAM945 gene, herein designated VGAM is inhibition of expression of VGAM945 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM945 correlate with, and may be deduced from, the identity of the target genes which VGAM945 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35512] Potassium Inwardly-rectifying Channel, Subfamily J, Member 1 (KCNJ1, Accession NM_000220) is a VGAM945 host target gene. KCNJ1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNJ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ1 BINDING SITE, designated SEQ ID:5727, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35513] A function of VGAM945 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 1 (KCNJ1, Accession NM_000220). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ1. Transcription Factor Dp-1 (TFDP1, Accession NM_007111) is another VGAM945 host target gene. TFDP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFDP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFDP1 BINDING SITE, designated SEQ ID:13977, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35514] Another function of VGAM945 is therefore inhibition of Transcription Factor Dp-1 (TFDP1, Accession NM_007111). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFDP1. Von Hippel-Lindau Binding Protein 1 (VBP1, Accession NM_003372) is another VGAM945 host target gene. VBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by VBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VBP1 BINDING SITE, designated SEQ ID:9400, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35515] Another function of VGAM945 is therefore inhibition of Von Hippel–Lindau Binding Protein 1 (VBP1, Accession NM_003372), a gene which binds specifically to cytosolic chaperonin (c-cpn) and transfers target proteins to it. Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VBP1. The function of VBP1 has been established by previous studies. Brinke et al. (1996) reported the presence of a novel inversion in the factor VIII (OMIM Ref. No. 306700) gene in hemophilic monozygotic twins. Brinke et al. (1996) noted that this novel inversion creates 2 hybrid transcription units. One of these is formed by the promoter and first exon of factor VIII and novel sequences. Brinke et al. (1997) determined that these novel sequences were part of the VBP1 gene. The VBP1 gene contains 6 exons and spans at least 30 kb. Northern blot

analysis revealed that VBP1 is ubiquitously expressed as a 1.7-kb mRNA and a much weaker 5.0-kb mRNA. By primer extension analysis, Brinke et al. (1997) found that there are 2 major and 1 minor transcription start sites. Brinke et al. (1997) cloned cDNAs of the mouse VBP1 homolog. The 160-amino acid mouse and human VBP1 protein sequences were identical. Clifford et al. (1999) could demonstrate no mutation in VBP1 in 89 sporadic cases of renal cell carcinoma. Hemberger et al. (1999) used the murine Vbp1 cDNA to investigate the expression of the Vbp1 mRNA in the mouse by in situ hybridization and Northern blot analysis. In fetal stages between days 9 and 18 of gestation, Vbp1 was expressed mainly in the central nervous system, retina, and liver. In addition, at day 12, high expression was observed in the labyrinthine region of the placenta. In later stage placentas, Vbp1 expression was, however, considerably reduced. Northern blot analysis of adult mouse tissues showed that Vbp1 was ubiquitously expressed. In situ analysis of several adult tissues showed that in most tissues the transcripts were evenly distributed. In brain, eye, kidney, and intestine, however, Vbp1 was expressed in specific cell types. In cerebellum and various tumors of VHL patients, no consistent differ-

ences in VBP1 expression levels could be detected between tumors characteristic of von Hippel–Lindau disease and normal tissue. Mapping of the murine Vbp1 gene revealed conserved chromosomal localization between mouse and human in a region homologous to human Xq28.

[35516] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35517] Brinke, A.; Tagliavacca, L.; Naylor, J.; Green, P.; Giangrande, P.; Giannelli, F. : Two chimaeric transcription units result from an inversion breaking intron 1 of the factor VIII gene and a region reportedly affected by reciprocal translocations in T–cell leukaemia. *Hum. Molec. Genet.* 5: 1945–1951, 1996. ; and

[35518] Hemberger, M.; Himmelbauer, H.; Neumann, H. P. H.; Plate, K. H.; Schwarzkopf, G.; Fundele, R. : Expression of the von Hippel–Lindau–binding protein–1 (Vbp1) in fetal and adult mouse tissue.

[35519] Further studies establishing the function and utilities of VBP1 are found in John Hopkins OMIM database record ID 300133, and in cited publications numbered 8945–8949 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. F-box Protein 30 (FBXO30, Accession NM_032145) is another VGAM945 host target gene. FBXO30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO30 BINDING SITE, designated SEQ ID:25839, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35520] Another function of VGAM945 is therefore inhibition of F-box Protein 30 (FBXO30, Accession NM_032145). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO30. FLJ23112 (Accession NM_024929) is another VGAM945 host target gene. FLJ23112 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23112 BINDING SITE, designated SEQ ID:24467, to the

nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35521] Another function of VGAM945 is therefore inhibition of FLJ23112 (Accession NM_024929). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23112. MGC13114 (Accession NM_032366) is another VGAM945 host target gene. MGC13114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13114 BINDING SITE, designated SEQ ID:26154, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35522] Another function of VGAM945 is therefore inhibition of MGC13114 (Accession NM_032366). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13114. Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842) is another VGAM945 host target gene. SPRY2 BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by SPRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPRY2 BINDING SITE, designated SEQ ID:12456, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35523] Another function of VGAM945 is therefore inhibition of Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPRY2. LOC144871 (Accession XM_096698) is another VGAM945 host target gene. LOC144871 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144871 BINDING SITE, designated SEQ ID:40470, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35524] Another function of VGAM945 is therefore inhibition of LOC144871 (Accession XM_096698). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144871. LOC145988 (Accession XM_085290) is another VGAM945 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38040, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35525] Another function of VGAM945 is therefore inhibition of LOC145988 (Accession XM_085290). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC219940 (Accession XM_167791) is another VGAM945 host target gene. LOC219940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219940, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219940 BINDING SITE, designated SEQ ID:44834, to the nucleotide sequence of VGAM945 RNA, herein designated VGAM RNA, also designated SEQ ID:3656.

[35526] Another function of VGAM945 is therefore inhibition of LOC219940 (Accession XM_167791). Accordingly, utilities of VGAM945 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219940. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 946 (VGAM946) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35527] VGAM946 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM946 was detected is described hereinabove with reference to Figs. 1–8.

[35528] VGAM946 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM946 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[35529] VGAM946 gene encodes a VGAM946 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM946 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM946 precursor RNA is designated SEQ ID:932, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:932 is located at position 80004 relative to the genome of Human Herpesvirus 6.

[35530] VGAM946 precursor RNA folds onto itself, forming VGAM946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35531] An enzyme complex designated DICER COMPLEX, `dices` the VGAM946 folded precursor RNA into VGAM946 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM946 RNA is designated SEQ ID:3657, and is provided hereinbelow with reference to the sequence listing part.

[35532] VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM946 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35533] VGAM946 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM946 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM946 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35534] The complementary binding of VGAM946 RNA, herein designated VGAM RNA, to host target binding sites on VGAM946 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM946 host target RNA into VGAM946 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[35535] It is appreciated that VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM946 host target genes. The mRNA of each one of this plurality of VGAM946 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM946 RNA, herein designated VGAM RNA, and which when bound by VGAM946 RNA causes inhibition of translation of respective one or more VGAM946 host target proteins.

[35536] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM946 gene, herein designated VGAM GENE, on one or more VGAM946 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35537] It is yet further appreciated that a function of VGAM946 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM946 correlate with, and may be deduced from, the identity of the host target genes which VGAM946 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35538] Nucleotide sequences of the VGAM946 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM946 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM946 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM946 are further described hereinbelow with reference to Table 1.

[35539] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM946 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM946 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35540] As mentioned hereinabove with reference to Fig. 1, a function of VGAM946 gene, herein designated VGAM is inhibition of expression of VGAM946 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM946 correlate with, and may be deduced from, the identity of the target genes which VGAM946 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35541] Cytoskeleton Associated Protein 2 (CKAP2, Accession NM_018204) is a VGAM946 host target gene. CKAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKAP2 BINDING SITE, designated SEQ ID:20088, to the nucleotide sequence of VGAM946 RNA, herein designated

VGAM RNA, also designated SEQ ID:3657.

[35542] A function of VGAM946 is therefore inhibition of Cytoskeleton Associated Protein 2 (CKAP2, Accession NM_018204). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKAP2. KIAA0427 (Accession NM_014772) is another VGAM946 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16574, to the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, also designated SEQ ID:3657.

[35543] Another function of VGAM946 is therefore inhibition of KIAA0427 (Accession NM_014772). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. MGC15705 (Accession NM_032757) is another VGAM946 host target gene. MGC15705 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MGC15705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15705 BINDING SITE, designated SEQ ID:26498, to the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, also designated SEQ ID:3657.

[35544] Another function of VGAM946 is therefore inhibition of MGC15705 (Accession NM_032757). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15705. Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255) is another VGAM946 host target gene. MRPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL10 BINDING SITE, designated SEQ ID:29769, to the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, also designated SEQ ID:3657.

[35545] Another function of VGAM946 is therefore inhibition of

Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL10. LOC220021 (Accession XM_167814) is another VGAM946 host target gene. LOC220021 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220021 BINDING SITE, designated SEQ ID:44851, to the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, also designated SEQ ID:3657.

[35546] Another function of VGAM946 is therefore inhibition of LOC220021 (Accession XM_167814). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220021. LOC91012 (Accession XM_035503) is another VGAM946 host target gene. LOC91012 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91012, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91012 BINDING SITE, designated SEQ ID:32278, to the nucleotide sequence of VGAM946 RNA, herein designated VGAM RNA, also designated SEQ ID:3657.

[35547] Another function of VGAM946 is therefore inhibition of LOC91012 (Accession XM_035503). Accordingly, utilities of VGAM946 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91012. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 947 (VGAM947) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35548] VGAM947 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM947 was detected is described hereinabove with reference to Figs. 1–8.

[35549] VGAM947 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM947 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[35550] VGAM947 gene encodes a VGAM947 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM947 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM947 precursor RNA is designated SEQ ID:933, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:933 is located at position 76244 relative to the genome of Human Herpesvirus 6.

[35551] VGAM947 precursor RNA folds onto itself, forming VGAM947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35552] An enzyme complex designated DICER COMPLEX, `dices` the VGAM947 folded precursor RNA into VGAM947 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM947 RNA is designated SEQ ID:3658, and is provided hereinbelow with reference to the sequence listing part.

[35553] VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM947 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35554] VGAM947 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM947 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM947 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35555] The complementary binding of VGAM947 RNA, herein designated VGAM RNA, to host target binding sites on VGAM947 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM947 host target RNA into VGAM947 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[35556] It is appreciated that VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM947 host target genes. The mRNA of each one of this plurality of VGAM947 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM947 RNA, herein designated VGAM RNA, and which when bound by VGAM947 RNA causes inhibition of translation of respective one or more VGAM947 host target proteins.

[35557] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM947 gene, herein designated VGAM GENE, on one or more VGAM947 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35558] It is yet further appreciated that a function of VGAM947 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM947 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM947 correlate with, and may be deduced from, the identity of the host target genes which VGAM947 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35559] Nucleotide sequences of the VGAM947 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM947 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM947 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM947 are further described hereinbelow with reference to Table 1.

[35560] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM947 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM947 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35561] As mentioned hereinabove with reference to Fig. 1, a function of VGAM947 gene, herein designated VGAM is inhibition of expression of VGAM947 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM947 correlate with, and may be deduced from, the identity of the target genes which VGAM947 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35562] Procollagen (type III) N-endopeptidase (PCOLN3, Accession NM_002768) is a VGAM947 host target gene. PCOLN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCOLN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCOLN3 BINDING SITE, designated SEQ ID:8661, to the nucleotide sequence of VGAM947 RNA,

herein designated VGAM RNA, also designated SEQ ID:3658.

[35563] A function of VGAM947 is therefore inhibition of Procollagen (type III) N-endopeptidase (PCOLN3, Accession NM_002768), a gene which is a member of the zincin superfamily of zinc-dependent metalloproteases. Accordingly, utilities of VGAM947 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCOLN3. The function of PCOLN3 has been established by previous studies. Metallopeptidases are a functionally diverse group of enzymes that are involved in critical stages of many biologic processes including bacterial pathogenesis, growth factor activation, and cancer metastasis. They are essential for the synthesis of the collagen that forms the fibrous scaffold of the extracellular matrix of tissues. Most metallopeptidases contain a zinc cation necessary for both structure coordination of the active site and catalysis. The zincin superfamily comprises metallopeptidases that contain the HEXXH zinc-binding consensus sequence. The 2 histidine residues serve as zinc ligands, and the glutamic acid residue polarizes a water molecule involved in the nucleophilic attack of peptide bonds. Subclassification is based on the identity of

other amino acids that act as zinc ligands. Gluzincins, for example, have glutamic acid as a third zinc ligand. Halila et al. (1989) isolated a possible cDNA for type III procollagen N-proteinase (OMIM Ref. No. PCOLN3) from a human placenta cDNA library. By screening a human placenta cDNA library with polyclonal antibodies raised against human PCOLN3 and the use of 5-prime RACE and primer extension strategies on the isolated cDNAs, Scott et al. (1996) identified a gene, which they symbolized PRSM1, that is a member of the gluzincin subfamily of metalloproteinases. The full-length composite sequence of the PRSM1 gene encodes a deduced 318-amino acid protein with an HELGH pentapeptide fitting the consensus sequence characteristic of zincins, and a glutamic acid 25 residues C-terminal of the first histidine, fitting the pattern of gluzincins for a third zinc-binding ligand. PRSM1 contains 3 clusters of cysteine residues: 1 cluster of 4 residues and 1 cluster of 6 residues at the N terminus and a cluster of 6 residues at the C terminus. However, the predicted sequence lacks potential glycosylation sites. Immunoblot analysis of placental tissue revealed an approximately 30-kD protein. Northern blot analysis of human fibroblast culture mRNA detected a transcript of approxi-

mately 2.5 kb. By Northern blot analysis, Nomura et al. (1994) found that PRSM1, which they designated KIAA0047, is expressed ubiquitously, with highest levels in lung and kidney as well as in HeLa and KG-1 cell lines.

[35564] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35565] Scott, I. C.; Halila, R.; Jenkins, J. M.; Mehan, S.; Apostolou, S.; Winqvist, R.; Callen, D. F.; Prockop, D. J.; Peltonen, L.; Kadler, K. E. : Molecular cloning, expression and chromosomal localization of a human gene encoding a 33 kDa putative metallopeptidase (PRSM1). *Gene* 174: 135-143, 1996. ; and

[35566] Nomura, N.; Nagase, T.; Miyajima, N.; Sazuka, T.; Tanaka, A.; Sato, S.; Seki, N.; Kawarabayasi, Y.; Ishikawa, K.; Tabata, S. : Prediction of the coding sequences of unidentified human ge.

[35567] Further studies establishing the function and utilities of PCOLN3 are found in John Hopkins OMIM database record ID 164010, and in cited publications numbered 2253-225 and 12737 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fig. 1 further provides a conceptual description of a novel bioin-

formatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 948 (VGAM948) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35568] VGAM948 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM948 was detected is described hereinabove with reference to Figs. 1–8.

[35569] VGAM948 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Carnation Italian Ringspot Virus. VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35570] VGAM948 gene encodes a VGAM948 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM948 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM948 precursor RNA is designated SEQ ID:934, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:934 is located at position 1710 relative to the genome of Carna–

tion Italian Ringspot Virus.

[35571] VGAM948 precursor RNA folds onto itself, forming VGAM948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35572] An enzyme complex designated DICER COMPLEX, `dices` the VGAM948 folded precursor RNA into VGAM948 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM948 RNA is designated SEQ ID:3659, and is provided hereinbelow with reference to the sequence listing part.

[35573] VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM948 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35574] VGAM948 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM948 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM948 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35575] The complementary binding of VGAM948 RNA, herein designated VGAM RNA, to host target binding sites on VGAM948 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM948 host target RNA into VGAM948 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35576] It is appreciated that VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM948 host target genes. The mRNA of each one of this plurality of VGAM948 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM948 RNA, herein designated VGAM RNA, and which when bound by VGAM948 RNA causes inhibition of translation of respective one or more VGAM948 host target proteins.

[35577] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM948 gene, herein designated VGAM GENE, on one or more VGAM948 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35578] It is yet further appreciated that a function of VGAM948 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of viral infection by Carnation Italian Ringspot Virus. Specific functions, and accordingly utilities, of

VGAM948 correlate with, and may be deduced from, the identity of the host target genes which VGAM948 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35579] Nucleotide sequences of the VGAM948 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM948 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM948 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM948 are further described hereinbelow with reference to Table 1.

[35580] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM948 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM948 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35581] As mentioned hereinabove with reference to Fig. 1, a function of VGAM948 gene, herein designated VGAM is inhibition of expression of VGAM948 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM948 correlate with, and may be deduced

from, the identity of the target genes which VGAM948 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35582] CD1A Antigen, A Polypeptide (CD1A, Accession XM_048792) is a VGAM948 host target gene. CD1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CD1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD1A BINDING SITE, designated SEQ ID:35271, to the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, also designated SEQ ID:3659.

[35583] A function of VGAM948 is therefore inhibition of CD1A Antigen, A Polypeptide (CD1A, Accession XM_048792), a gene which is involved in antigen presentation. Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD1A. The function of CD1A has been established by previous studies. Thymocyte antigens CD1 were thought to be human counterparts of mouse thymus leukemia (TL) antigens (OMIM Ref. No. 188850). Serological and biochemical analyses indicated the existence of at

least 3 subsets, the first of which was initially identified by a monoclonal antibody. Like TL antigens, CD1 antigens are expressed on cortical thymocytes, as well as on some lymphoid neoplasias, and resemble in structure the major histocompatibility complex class I antigens. (CD in the nomenclature of these cell surface antigens is derived from 'cluster of differentiation.')

The expression of surface markers correlates with the stage of differentiation of lymphocytes, hence they were referred to as differentiation markers and proved to be powerful tools for identification, characterization, and analysis. The concept of differentiation markers, although derived from studies on lymphocytes, has greater applicability. For example, the developing embryo has stage-specific markers, and many other developing systems can be studied by utilizing unique markers at certain stages of differentiation. Monoclonal antibodies facilitated greatly the identification of lymphocyte differentiation antigens; it also brought about a Tower of Babel in nomenclature as discoverers of new markers gave them new names without regard to possible identity to previously described antigens. In 1982, the First International Workshop in Human Leukocyte Differentiation Antigens was held in Paris. At that meeting, 139

monoclonal antibodies were tested by immunofluorescence, and the antibodies were grouped into 'clusters' on the basis of the results. At the Fifth International Congress of Immunology, held in Kyoto, Japan, in 1983, the nomenclature subcommittee officially adopted this scheme of nomenclature. The idea of the 'cluster of differentiation' was to group all known antibodies that reacted with the same marker. When new antigens are discovered, they are sometimes said to be 'clustered' when their relationship to other CDs has been determined. CD4 (OMIM Ref. No. 186940) and CD8 (OMIM Ref. No. 186910) are at the heart of many immunologic mechanisms. Park and Bendelac (2000) noted that the crystal structure of murine CD1D (see OMIM Ref. No. Zeng et al., 1997), showing a deep ligand-binding groove made of 2 large electrostatically neutral pockets lined with clustered hydrophobic residues, appears to suggest a way in which CD1 molecules, which complex with B2M (OMIM Ref. No. 109700), bind lipids. Park and Bendelac (2000) also observed that the stable lipid binding might occur in the secretory pathway, at the cell surface, or only after internalization in an acidified compartment. The intracellular locations include different compartments of the endocytic pathway: CD1A is concen-

trated in the early or recycling endosome, CD1B and CD1D in the late endosome or lysosome, and CD1C in the late endosome. Access to the endocytic pathway is regulated by a tyrosine-based motif in the cytoplasmic tail of CD1 that differs among CD1B, CD1C, and CD1D.

[35584] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35585] Park, S.-H.; Bendelac, A. : CD1-restricted T-cell responses and microbial infection. *Nature* 406: 788–792, 2000. ; and

[35586] Martin, L. H.; Calabi, F.; Milstein, C. : Isolation of CD1 genes: a family of major histocompatibility complex-related differentiation antigens. *Proc. Nat. Acad. Sci.* 83: 9154–9158, 198.

[35587] Further studies establishing the function and utilities of CD1A are found in John Hopkins OMIM database record ID 188370, and in cited publications numbered 10280–10282, 10428–10430, 393 and 10279–5696 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deleted In Lymphocytic Leukemia, 2 (DLEU2, Accession NM_006021) is another VGAM948 host target gene. DLEU2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by DLEU2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLEU2 BINDING SITE, designated SEQ ID:12638, to the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, also designated SEQ ID:3659.

[35588] Another function of VGAM948 is therefore inhibition of Deleted In Lymphocytic Leukemia, 2 (DLEU2, Accession NM_006021). Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLEU2. Eukaryotic Translation Elongation Factor 1 Beta 2 (EEF1B2, Accession NM_001959) is another VGAM948 host target gene. EEF1B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EEF1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EEF1B2 BINDING SITE, designated SEQ ID:7682, to the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, also designated SEQ ID:3659.

[35589] Another function of VGAM948 is therefore inhibition of Eukaryotic Translation Elongation Factor 1 Beta 2 (EEF1B2, Accession NM_001959), a gene which stimulates the exchange of gdp bound to ef-1-alpha to gtp (by similarity). Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EEF1B2. The function of EEF1B2 has been established by previous studies. Sanders et al. (1991) identified a human cDNA by hybridization with a pig EF-1 beta probe. The gene was subsequently mapped by Pizzuti et al. (1993) to chromosome 2 by PCR analysis of a somatic cell hybrid DNA panel. The gene is referred to here as 'isoform 2a' of EEF1-beta because of its chromosome 2 location.

[35590] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35591] Pizzuti, A.; Gennarelli, M.; Novelli, G.; Colosimo, A.; Cicero, S. L.; Caskey, C. T.; Dallapiccola, B. : Human elongation factor EF-1-beta: cloning and characterization of the EF1-beta-5a gene and assignment of EF-1-beta isoforms to chromosomes 2, 5, 15 and X. Biochem. Biophys. Res. Commun. 197: 154-162, 1993. ; and

[35592] Sanders, J.; Maassen, J. A.; Amons, R.; Moller, W. : Nucleotide sequence of human elongation factor-1-beta cDNA. Nucleic Acids Res. 19: 4551, 1991.

[35593] Further studies establishing the function and utilities of EEF1B2 are found in John Hopkins OMIM database record ID 600655, and in cited publications numbered 87 and 7930 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM_002065) is another VGAM948 host target gene. GLUL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUL BINDING SITE, designated SEQ ID:7834, to the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, also designated SEQ ID:3659.

[35594] Another function of VGAM948 is therefore inhibition of Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM_002065), a gene which catalyzes the condensation of glutamate and ammonia to form glutamine.

Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUL. The function of GLUL has been established by previous studies. Glutamine synthetase (EC 6.3.1.2), also called glutamate–ammonia ligase (GLUL), is expressed throughout the body and plays an important role in controlling body pH and in removing ammonia from the circulation. The enzyme clears L–glutamate, the major neurotransmitter in the central nervous system, from neuronal synapses (see OMIM Ref. No. references in Clancy et al., 1996). Gibbs et al. (1987) reported the complete 1,119–bp coding sequence of glutamine synthetase, which they determined from a liver–derived cDNA. Pesole et al. (1991) suggested that glutamine synthetase is a good molecular clock for determining times of divergence even as great as that which occurred between eukaryotes and prokaryotes. One conclusion reached by Pesole et al. (1991) was that organelle–specific enzymes, such as those of the mitochondria, may have originated from a duplication of nuclear genes. The endosymbiotic hypothesis suggests that a transfer of prokaryotic genes to nuclei occurred during the evolution of the primitive eukaryotic cell. In some cases, it is likely that the old prokaryotic

gene could not be active in the new nuclear genome environment and was totally lost because its function in the organelle could be dispensed with. Subsequently, a new organelle-specific enzyme could have originated to serve specialized metabolic functions. The presence of glutamine synthetase in mitochondria is linked to the nitrogen metabolism of the species, and in particular to the need for glutamine as a source of ammonia and for particular biochemical pathways for ammonia detoxification.

[35595] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35596] Gibbs, C. S.; Campbell, K. E.; Wilson, R. H. : Sequence of a human glutamine synthetase cDNA. *Nucleic Acids Res.* 15: 6293 only, 1987. ; and

[35597] Pesole, G.; Bozzetti, M. P.; Lanave, C.; Preparata, G.; Saccone, C. : Glutamine synthetase gene evolution: a good molecular clock. *Proc. Nat. Acad. Sci.* 88: 522–526, 1991.

[35598] Further studies establishing the function and utilities of GLUL are found in John Hopkins OMIM database record ID 138290, and in cited publications numbered 2012–2017 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC220753

(Accession XM_167549) is another VGAM948 host target gene. LOC220753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220753 BINDING SITE, designated SEQ ID:44660, to the nucleotide sequence of VGAM948 RNA, herein designated VGAM RNA, also designated SEQ ID:3659.

[35599] Another function of VGAM948 is therefore inhibition of LOC220753 (Accession XM_167549). Accordingly, utilities of VGAM948 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220753. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 949 (VGAM949) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35600] VGAM949 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM949 was detected is described hereinabove with reference to Figs. 1–8.

[35601] VGAM949 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Carnation Italian Ringspot Virus. VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35602] VGAM949 gene encodes a VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM949 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM949 precursor RNA is designated SEQ ID:935, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:935 is located at position 2039 relative to the genome of Carnation Italian Ringspot Virus.

[35603] VGAM949 precursor RNA folds onto itself, forming VGAM949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35604] An enzyme complex designated DICER COMPLEX, `dices` the VGAM949 folded precursor RNA into VGAM949 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM949 RNA is designated SEQ ID:3660, and is provided hereinbelow with reference to the sequence listing part.

[35605] VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM949 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35606] VGAM949 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM949 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM949 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[35607] The complementary binding of VGAM949 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM949 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM949 host target RNA into VGAM949 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35608] It is appreciated that VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM949 host target genes. The mRNA of each one of this plurality of VGAM949 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM949 RNA, herein designated VGAM RNA, and which when bound by VGAM949 RNA causes inhibition of translation of respective one or more VGAM949 host target proteins.

[35609] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM949 gene, herein designated VGAM GENE, on one or more VGAM949 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35610] It is yet further appreciated that a function of VGAM949 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of viral infection by Carnation Italian Ringspot Virus. Specific functions, and accordingly utilities, of VGAM949 correlate with, and may be deduced from, the identity of the host target genes which VGAM949 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35611] Nucleotide sequences of the VGAM949 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM949 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM949 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM949 are further described hereinbelow with reference to Table 1.

[35612] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM949 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM949 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35613] As mentioned hereinabove with reference to Fig. 1, a function of VGAM949 gene, herein designated VGAM is inhibition of expression of VGAM949 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM949 correlate with, and may be deduced from, the identity of the target genes which VGAM949 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35614] APM1 (Accession NM_004797) is a VGAM949 host target gene. APM1 BINDING SITE1 and APM1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by APM1, corresponding to HOST TAR-

GET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APM1 BINDING SITE1 and APM1 BINDING SITE2, designated SEQ ID:11206 and SEQ ID:11212 respectively, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35615] A function of VGAM949 is therefore inhibition of APM1 (Accession NM_004797). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APM1. Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357) is another VGAM949 host target gene. CASP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP8 BINDING SITE, designated SEQ ID:27205, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35616] Another function of VGAM949 is therefore inhibition of

Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM145. Coronin, Actin Binding Protein, 1C (CORO1C, Accession NM_014325) is another VGAM949 host target gene. CORO1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORO1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO1C BINDING SITE, designated SEQ ID:15628, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35617] Another function of VGAM949 is therefore inhibition of Coronin, Actin Binding Protein, 1C (CORO1C, Accession

NM_014325). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CORO1C. DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM_006892) is another VGAM949 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13759, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35618] Another function of VGAM949 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM280. Eukaryotic Translation Initiation Factor 3, Subunit 10 Theta, 150/170kDa (EIF3S10, Accession XM_049795) is another VGAM949 host target gene. EIF3S10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF3S10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF3S10 BINDING SITE, designated SEQ ID:35502, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35619] Another function of VGAM949 is therefore inhibition of Eukaryotic Translation Initiation Factor 3, Subunit 10 Theta, 150/170kDa (EIF3S10, Accession XM_049795), a gene which binds to the 40s ribosome and promotes the binding of methionyl-trnai and mrna. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF3S10. The function of EIF3S10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM882. FAT Tumor Suppressor Homolog 2

(Drosophila) (FAT2, Accession NM_001447) is another VGAM949 host target gene. FAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAT2 BINDING SITE, designated SEQ ID:7174, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35620] Another function of VGAM949 is therefore inhibition of FAT Tumor Suppressor Homolog 2 (Drosophila) (FAT2, Accession NM_001447), a gene which could function as a cell-adhesion protein. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAT2. The function of FAT2 has been established by previous studies. The domain that characterizes epidermal growth factor (EGF; 131530) consists of approximately 50 amino acids with 3 disulfide bonds. EGF-like domains are believed to play a critical role in a number of extracellular events, including cell adhesion and receptor-ligand interactions. Proteins with EGF-like domains often consist of more than 1,000

amino acids, have multiple copies of the EGF-like domain, and contain additional domains known to be involved in specific protein-protein interactions. To identify proteins containing EGF-like domains, Nakayama et al. (1998) searched a database of long cDNA sequences randomly selected from a human brain cDNA library for those that encode an EGF-like motif. They identified several partial cDNAs encoding novel proteins with EGF-like domains, such as FAT2, which they named MEGF1. Nakayama et al. (1998) isolated a rat cDNA containing the complete Megf1 coding sequence. The predicted Megf1 protein has a signal sequence, 34 cadherin motifs (see OMIM Ref. No. 603006), a laminin G domain (see OMIM Ref. No. 601033), 2 EGF-like domains, a transmembrane domain, a cytoplasmic proline-rich sequence, and a cytoplasmic RGD (arginine-glycine-aspartic acid) motif, which is found in proteins modulating cell adhesion. The predicted structure of Megf1 is similar overall to the structures of the Drosophila 'fat' gene product and human FAT (OMIM Ref. No. 600976), although the number of EGF-like domains varies among these proteins. The Drosophila fat gene is a tumor suppressor gene whose product controls cell proliferation and morphogenesis in the imaginal discs in a

contact-dependent manner. Northern blot analysis of various regions of rat brain detected Megf1 expression only in the cerebellum.

[35621] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35622] Nakayama, M.; Nakajima, D.; Nagase, T.; Nomura, N.; Seki, N.; Ohara, O. : Identification of high-molecular-weight proteins with multiple EGF-like motifs by motif-trap screening. *Genomics* 51: 27-34, 1998. ; and

[35623] Wu, Q.; Maniatis, T. : Large exons encoding multiple ectodomains are a characteristic feature of protocadherin genes. *Proc. Nat. Acad. Sci.* 97: 3124-3129, 2000.

[35624] Further studies establishing the function and utilities of FAT2 are found in John Hopkins OMIM database record ID 604269, and in cited publications numbered 7437-7438 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nucleosome Assembly Protein 1-like 4 (NAP1L4, Accession NM_005969) is another VGAM949 host target gene. NAP1L4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAP1L4, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAP1L4 BINDING SITE, designated SEQ ID:12589, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35625] Another function of VGAM949 is therefore inhibition of Nucleosome Assembly Protein 1-like 4 (NAP1L4, Accession NM_005969), a gene which may have a role as a histone chaperone. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAP1L4. The function of NAP1L4 has been established by previous studies. Hu et al. (1996) used a positional cloning approach to isolate a gene which is located 100 kb centromeric to the proximal Beckwith–Wiedemann breakpoint cluster region (BWS; 130650) on chromosome 11p15. This gene is homologous to the yeast nucleosome assembly protein NAP1 (OMIM Ref. No. 164060). The authors designated the new gene NAP2. They demonstrated that this gene shows biallelic expression in all tissues tested and that it therefore diverges in its expression from IGF2 (OMIM Ref. No. 147470), H19 (OMIM Ref. No. 103280), and p57(KIP2) (OMIM Ref. No. 600856), which also map to 11p15.5 in

the vicinity of the BWS gene. The NAP2 gene encodes a highly acidic protein of 375 amino acids. A 1,200-bp 3-prime untranslated region was present. Rodriguez et al. (1997) reported that the NAP1L4 gene consists of 14 exons and spans approximately 30.5 kb. Histones are thought to play a key role in regulating gene expression at the level of DNA packaging. The deduced amino acid sequence of NAP2 indicates that it is a protein with a potential nuclear localization motif and 2 clusters of highly acidic residues. By functional analysis of recombinant NAP2 protein purified from *Escherichia coli*, Rodriguez et al. (1997) found that this protein can interact with both core and linker histones (see OMIM Ref. No. 142709). They demonstrated that recombinant NAP2 can transfer histones onto naked DNA templates. Subcellular localization studies of NAP2 indicated that it can shuttle between the cytoplasm and nucleus, suggesting a role as a histone chaperone. NAP1L4 maps to a region implicated in Wilms tumor etiology (see OMIM Ref. No. 194071). Rodriguez et al. (1997) analyzed the gene encoding NAP2 for mutations and found no evidence of nonsense, frameshift, or deletion mutations. Their findings, coupled with tumor suppression assays in Wilms tumor cells, did not support a

role for NAP2 in the etiology of that neoplasm.

[35626] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35627] Hu, R.-J.; Lee, M. P.; Johnson, L. A.; Feinberg, A. P. : A novel human homologue of yeast nucleosome assembly protein, 65 kb centromeric to the p57(KIP2) gene, is biallelically expressed in fetal and adult tissues. Hum. Molec. Genet. 5: 1743–1748, 1996. ; and

[35628] Rodriguez, P.; Munroe, D.; Prawitt, D.; Chu, L. L.; Bric, E.; Kim, J.; Reid, L. H.; Davies, C.; Nakagama, H.; Loebbert, R.; Winterpacht, A.; Petruzzi, M.-J.; Higgins, M. J.; Nowak, N.;

[35629] Further studies establishing the function and utilities of NAP1L4 are found in John Hopkins OMIM database record ID 601651, and in cited publications numbered 6557–6558 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768) is another VGAM949 host target gene. PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9845, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35630] Another function of VGAM949 is therefore inhibition of Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768), a gene which is a phosphoprotein and involved in glucose uptake. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 has been established by previous studies. Astrocytes are involved in a variety of functions, including storage of glycogen and support for the migration and differentiation of neurons. They express membrane receptors which allow them to respond to extracellular signals. Activation of the receptors induces a cascade of events, such as the stimulation of protein kinases and the subsequent phosphorylation of target proteins. Araujo et al. (1993) identified a unique 15-kD protein in astrocytes that exists as a nonphosphorylated form and as 2 increasingly phosphorylated varieties. This protein, which they called PEA15, contains a consensus site for protein

kinase C (PKC; e.g., 176960) and is an endogenous substrate for PKC. Using differential display to identify genes whose expressions are altered in tissues derived from type II diabetes mellitus (OMIM Ref. No. 125853) patients compared with nondiabetic individuals, Condorelli et al. (1998) cloned cDNAs encoding PEA15, which they named PED for 'phosphoprotein enriched in diabetes'. The ubiquitously expressed 2.8-kb PED mRNA was overexpressed in fibroblasts, skeletal muscle, and adipose tissue from type II diabetics. Levels of the 15-kD PED phosphoprotein were also elevated in type II diabetic tissues. The authors demonstrated that transfection of a PED cDNA into differentiating L6 skeletal muscle cells increases the content of glucose transporter-1 (GLUT1; 138140) on the plasma membrane and inhibits insulin-stimulated glucose transport and cell surface recruitment of glucose transporter-4 (GLUT4; 138190). These effects were reversed by blocking PKC activity.

[35631] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35632] Araujo, H.; Danziger, N.; Cordier, J.; Glowinski, J.; Chneiweiss, H. : Characterization of PEA-15, a major substrate

for protein kinase C in astrocytes. J. Biol. Chem. 268: 5911–5920, 1993. ; and

[35633] Condorelli, G.; Vigliotta, G.; Iavarone, C.; Caruso, M.; Tocchi, C. G.; Andreozzi, F.; Cafieri, A.; Tecce, M. F.; Formisano, P.; Beguinot, L.; Beguinot, F. : PED/PEA-15 gene controls.

[35634] Further studies establishing the function and utilities of PEA15 are found in John Hopkins OMIM database record ID 603434, and in cited publications numbered 5348–5354 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Peanut-like 2 (Drosophila) (PNUTL2, Accession NM_080417) is another VGAM949 host target gene. PNUTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PNUTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNUTL2 BINDING SITE, designated SEQ ID:27836, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35635] Another function of VGAM949 is therefore inhibition of

Peanut-like 2 (Drosophila) (PNUTL2, Accession NM_080417), a gene which is involved in cytokinesis. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNUTL2. The function of PNUTL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281) is another VGAM949 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42832, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35636] Another function of VGAM949 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SCN1A. Sialyltransferase 4C (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4C, Accession NM_006278) is another VGAM949 host target gene. SIAT4C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT4C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT4C BINDING SITE, designated SEQ ID:12957, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35637] Another function of VGAM949 is therefore inhibition of Sialyltransferase 4C (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4C, Accession NM_006278), a gene which may be involved in the biosynthesis of the sialyl lewis x determinant. Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT4C. The function of SIAT4C has been established by previous studies. The synthesis of alpha-2,3-linked sialic acid to Gal(beta-1,3)GalNAc is mediated by at least 3 beta-galactoside alpha-2,3-sialyltransferases (EC 2.4.99.4),

SiaT-4, that are encoded by 3 distinct genes. In contrast, only a single gene encodes the beta-galactoside alpha-2,6-sialyltransferase (EC 2.4.99.1), SiaT-1. Chang et al. (1995) assessed the relationship and nature of the SiaT-4 genes. Analysis of human-mouse somatic cell hybrids demonstrated that the sialyltransferase genes are dispersed in the human genome. One gene, SiaT-4a, resides in chromosome 8; that for SiaT-4b resides in 1p34-p21; and that for SiaT-4c, in 11q23.3-qter. The gene symbols for these genes were designated SIAT4A (OMIM Ref. No. 607187), SIAT4B (OMIM Ref. No. 607188), and SIAT4C, respectively. Kitagawa et al. (1996) described the chromosomal mapping and genomic organization of the human alpha-2,3-sialyltransferase gene. They mapped the gene to 11q23-q24 by isotopic in situ hybridization to metaphase chromosomes. They showed that it spans more than 25 kb of human genomic DNA and is distributed over 14 exons that range in size from 61 to 679 bp. Previous characterization of cDNAs encoding this enzyme revealed that the gene produces at least 3 transcripts in human placenta, which code for identical protein sequences except at the 5-prime ends. Further screening for clones that contained the 5-prime end of

the cDNA identified 2 additional distinct mRNAs that are expressed in human placenta. Comparison of the genomic DNA sequence with that of the 5 different mRNAs indicated that these transcripts are produced by a combination of alternative splicing and alternative promoter utilization. Northern analysis indicated that one of them is specifically expressed in placenta, testis, and ovary, indicating that its expression is independently regulated from the others.

[35638] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35639] Chang, M.-L.; Eddy, R. L.; Shows, T. B.; Lau, J. T. Y. : Three genes that encode human beta-galactoside alpha-2,3-sialyltransferases. Structural analysis and chromosomal mapping studies. *Glycobiology* 5: 319-325, 1995. ; and

[35640] Kitagawa, H.; Mattei, M.-G.; Paulson, J. C. : Genomic organization and chromosomal mapping of the Gal-beta-1,3GalNAc/Gal-beta-1,4GlcNAc alpha-2,3-sialyltransferase. *J. Biol. Chem.* 271: 931.

[35641] Further studies establishing the function and utilities of SIAT4C are found in John Hopkins OMIM database record

ID 104240, and in cited publications numbered 475–47 and 474 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM_000441) is another VGAM949 host target gene. SLC26A4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC26A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A4 BINDING SITE, designated SEQ ID:6028, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35642] Another function of VGAM949 is therefore inhibition of Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM_000441). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A4. CDK5 Regulatory Subunit Associated Protein 3 (CDK5RAP3, Accession NM_025197) is another VGAM949 host target gene. CDK5RAP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by

CDK5RAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK5RAP3 BINDING SITE, designated SEQ ID:24852, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35643] Another function of VGAM949 is therefore inhibition of CDK5 Regulatory Subunit Associated Protein 3 (CDK5RAP3, Accession NM_025197). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK5RAP3. DIS3 (Accession NM_014953) is another VGAM949 host target gene. DIS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIS3 BINDING SITE, designated SEQ ID:17298, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35644] Another function of VGAM949 is therefore inhibition of

DIS3 (Accession NM_014953). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIS3.

FLJ11113 (Accession XM_002359) is another VGAM949 host target gene. FLJ11113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11113 BINDING SITE, designated SEQ ID:29875, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35645] Another function of VGAM949 is therefore inhibition of FLJ11113 (Accession XM_002359). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11113. FLJ21324 (Accession XM_165988) is another VGAM949 host target gene. FLJ21324 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21324, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ21324 BINDING SITE, designated SEQ ID:43828, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35646] Another function of VGAM949 is therefore inhibition of FLJ21324 (Accession XM_165988). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21324. FLJ21918 (Accession NM_024939) is another VGAM949 host target gene. FLJ21918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21918 BINDING SITE, designated SEQ ID:24482, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35647] Another function of VGAM949 is therefore inhibition of FLJ21918 (Accession NM_024939). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21918. KIAA0254 (Accession NM_014758) is another VGAM949

host target gene. KIAA0254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0254 BINDING SITE, designated SEQ ID:16504, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35648] Another function of VGAM949 is therefore inhibition of KIAA0254 (Accession NM_014758). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0254. KIAA0258 (Accession NM_014785) is another VGAM949 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16641, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35649] Another function of VGAM949 is therefore inhibition of KIAA0258 (Accession NM_014785). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA0828 (Accession XM_088105) is another VGAM949 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39513, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35650] Another function of VGAM949 is therefore inhibition of KIAA0828 (Accession XM_088105). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM_003010) is another VGAM949 host target gene. MAP2K4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAP2K4, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K4 BINDING SITE, designated SEQ ID:8916, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35651] Another function of VGAM949 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 4 (MAP2K4, Accession NM_003010). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K4. Trinucleotide Repeat Containing 6 (TNRC6, Accession XM_047123) is another VGAM949 host target gene. TNRC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TNRC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC6 BINDING SITE, designated SEQ ID:34899, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35652] Another function of VGAM949 is therefore inhibition of

Trinucleotide Repeat Containing 6 (TNRC6, Accession XM_047123). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC6. TU12B1-TY (Accession NM_016575) is another VGAM949 host target gene. TU12B1-TY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU12B1-TY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU12B1-TY BINDING SITE, designated SEQ ID:18642, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35653] Another function of VGAM949 is therefore inhibition of TU12B1-TY (Accession NM_016575). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TU12B1-TY. LOC115297 (Accession XM_053313) is another VGAM949 host target gene. LOC115297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115297, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115297 BINDING SITE, designated SEQ ID:36068, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35654] Another function of VGAM949 is therefore inhibition of LOC115297 (Accession XM_053313). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115297. LOC147165 (Accession XM_097205) is another VGAM949 host target gene. LOC147165 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147165 BINDING SITE, designated SEQ ID:40812, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35655] Another function of VGAM949 is therefore inhibition of LOC147165 (Accession XM_097205). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC147165. LOC150605 (Accession XM_097927) is another VGAM949 host target gene. LOC150605 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150605, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150605 BINDING SITE, designated SEQ ID:41230, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35656] Another function of VGAM949 is therefore inhibition of LOC150605 (Accession XM_097927). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150605. LOC169436 (Accession XM_095696) is another VGAM949 host target gene. LOC169436 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169436, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169436 BINDING SITE, designated SEQ ID:40278, to the nucleotide sequence of VGAM949 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3660.

[35657] Another function of VGAM949 is therefore inhibition of LOC169436 (Accession XM_095696). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169436. LOC170425 (Accession XM_084330) is another VGAM949 host target gene. LOC170425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170425 BINDING SITE, designated SEQ ID:37550, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35658] Another function of VGAM949 is therefore inhibition of LOC170425 (Accession XM_084330). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170425. LOC220729 (Accession XM_049575) is another VGAM949 host target gene. LOC220729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220729, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220729 BINDING SITE, designated SEQ ID:35449, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35659] Another function of VGAM949 is therefore inhibition of LOC220729 (Accession XM_049575). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220729. LOC255031 (Accession XM_173187) is another VGAM949 host target gene. LOC255031 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255031 BINDING SITE, designated SEQ ID:46431, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35660] Another function of VGAM949 is therefore inhibition of LOC255031 (Accession XM_173187). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC255031. LOC257422 (Accession XM_172923) is another VGAM949 host target gene. LOC257422 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257422 BINDING SITE, designated SEQ ID:46191, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35661] Another function of VGAM949 is therefore inhibition of LOC257422 (Accession XM_172923). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257422. LOC91272 (Accession XM_037317) is another VGAM949 host target gene. LOC91272 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91272, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91272 BINDING SITE, designated SEQ ID:32613, to the

nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35662] Another function of VGAM949 is therefore inhibition of LOC91272 (Accession XM_037317). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91272. LOC93512 (Accession XM_051758) is another VGAM949 host target gene. LOC93512 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93512 BINDING SITE, designated SEQ ID:35876, to the nucleotide sequence of VGAM949 RNA, herein designated VGAM RNA, also designated SEQ ID:3660.

[35663] Another function of VGAM949 is therefore inhibition of LOC93512 (Accession XM_051758). Accordingly, utilities of VGAM949 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93512. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 950 (VGAM950) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35664] VGAM950 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM950 was detected is described hereinabove with reference to Figs. 1–8.

[35665] VGAM950 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Bushy Stunt Virus. VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35666] VGAM950 gene encodes a VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM950 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM950 precursor RNA is designated SEQ ID:936, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:936 is located at position 3278 relative to the genome of Tomato Bushy Stunt Virus.

[35667] VGAM950 precursor RNA folds onto itself, forming VGAM950 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35668] An enzyme complex designated DICER COMPLEX, `dices` the VGAM950 folded precursor RNA into VGAM950 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM950 RNA is designated SEQ ID:3661, and is provided hereinbelow with reference to the sequence listing part.

[35669] VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM950 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM950 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35670] VGAM950 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM950 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM950 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35671] The complementary binding of VGAM950 RNA, herein designated VGAM RNA, to host target binding sites on VGAM950 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM950 host target RNA into VGAM950 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35672] It is appreciated that VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM950 host target genes. The mRNA of each one of this plurality of VGAM950 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM950 RNA, herein designated VGAM RNA, and which when bound by VGAM950 RNA causes inhibition of translation of respective one or more VGAM950 host target proteins.

[35673] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM950 gene, herein designated VGAM GENE, on one or more VGAM950 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35674] It is yet further appreciated that a function of VGAM950 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM950 include diagnosis, prevention and treatment of viral infection by Tomato Bushy Stunt Virus. Specific functions, and accordingly utilities, of VGAM950 correlate with, and may be deduced from, the identity of

the host target genes which VGAM950 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35675] Nucleotide sequences of the VGAM950 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM950 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM950 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM950 are further described hereinbelow with reference to Table 1.

[35676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM950 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM950 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35677] As mentioned hereinabove with reference to Fig. 1, a function of VGAM950 gene, herein designated VGAM is inhibition of expression of VGAM950 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM950 correlate with, and may be deduced from, the identity of the target genes which VGAM950

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35678] RIG (Accession NM_006394) is a VGAM950 host target gene. RIG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIG BINDING SITE, designated SEQ ID:13106, to the nucleotide sequence of VGAM950 RNA, herein designated VGAM RNA, also designated SEQ ID:3661.

[35679] A function of VGAM950 is therefore inhibition of RIG (Accession NM_006394), a gene which is ribosomal protein S15. Accordingly, utilities of VGAM950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIG. The function of RIG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130) is another VGAM950 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLPH3, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLPH3 BINDING SITE, designated SEQ ID:22684, to the nucleotide sequence of VGAM950 RNA, herein designated VGAM RNA, also designated SEQ ID:3661.

[35680] Another function of VGAM950 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130). Accordingly, utilities of VGAM950 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLPH3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 951 (VGAM951) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35681] VGAM951 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM951 was detected is described hereinabove with reference to Figs. 1–8.

[35682] VGAM951 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Bushy Stunt Virus. VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35683] VGAM951 gene encodes a VGAM951 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM951 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM951 precursor RNA is designated SEQ ID:937, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:937 is located at position 1675 relative to the genome of Tomato Bushy Stunt Virus.

[35684] VGAM951 precursor RNA folds onto itself, forming VGAM951 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35685] An enzyme complex designated DICER COMPLEX, `dices` the VGAM951 folded precursor RNA into VGAM951 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM951 RNA is designated SEQ ID:3662, and is provided hereinbelow with reference to the sequence listing part.

[35686] VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM951 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[35687] VGAM951 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM951 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM951 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35688] The complementary binding of VGAM951 RNA, herein designated VGAM RNA, to host target binding sites on VGAM951 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM951 host target RNA into VGAM951 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35689] It is appreciated that VGAM951 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM951 host target genes. The mRNA of each one of this plurality of VGAM951 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM951 RNA, herein designated VGAM RNA, and which when bound by VGAM951 RNA causes inhibition of translation of respective one or more VGAM951 host target proteins.

[35690] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM951 gene, herein designated VGAM GENE, on one or more VGAM951 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35691] It is yet further appreciated that a function of VGAM951 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM951 include diagnosis, prevention and treatment of viral infection by Tomato Bushy Stunt Virus. Specific functions, and accordingly utilities, of VGAM951 correlate with, and may be deduced from, the identity of the host target genes which VGAM951 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35692] Nucleotide sequences of the VGAM951 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM951 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM951 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM951 are further
described hereinbelow with reference to Table 1.

[35693] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM951 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM951 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[35694] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM951 gene, herein designated VGAM is
inhibition of expression of VGAM951 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM951 correlate with, and may be deduced
from, the identity of the target genes which VGAM951
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[35695] Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession
NM_000134) is a VGAM951 host target gene. FABP2 BIND-

ING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FABP2 BINDING SITE, designated SEQ ID:5623, to the nucleotide sequence of VGAM951 RNA, herein designated VGAM RNA, also designated SEQ ID:3662.

[35696] A function of VGAM951 is therefore inhibition of Fatty Acid Binding Protein 2, Intestinal (FABP2, Accession NM_000134), a gene which may have a role in dietary fat uptake or processing. Accordingly, utilities of VGAM951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FABP2. The function of FABP2 has been established by previous studies. To test the hypothesis that the A54T FABP2 polymorphism is associated with impaired lipid metabolism and cardiovascular disease, Carlsson et al. (2000) compared clinical characteristics and a parental history of cardiovascular disease between 213 sib pairs discordant for the polymorphism. Sibs with an excess of the thr54 allele had higher triglyceride and cholesterol concentrations than sibs with the ala54 allele. Parents of offspring with the

thr/thr and thr/ala genotypes reported an increased prevalence of stroke compared to parents of offspring with the ala/ala genotype. The authors confirmed the association of the FABP2 thr54 allele with increased concentrations of cholesterol and triglycerides in genotype-discordant sib pairs. They also presented novel evidence that genetic variation in the FABP2 gene may increase susceptibility to stroke. To assess whether increased intestinal triglyceride input leads to elevated fasting and postprandial triglycerides in type 2 diabetes (NIDDM), Georgopoulos et al. (2000) studied the ala54-to-thr polymorphism of FABP2, which is associated with increased intestinal input of triglyceride. Of the 287 diabetic patients screened, 108 (37.6%) were heterozygous and 31 (10.8%) were homozygous for the thr54 allele. Mean fasting plasma triglyceride levels in patients with the wild-type (OMIM Ref. No. n = 80), those heterozygous for the thr54 allele (OMIM Ref. No. n = 57), and those homozygous for it (OMIM Ref. No. n = 18) were 2.0 ± 0.09 , 2.7 ± 0.20 , and 3.8 ± 0.43 mmol/L, respectively. A linear relationship of mean fasting plasma triglyceride levels between the 3 groups was found. After fat ingestion, the postprandial area under the curve of plasma triglyceride and chy-

lomicrons was higher in the thr54/thr54 (n = 6) than in the wild-type (n = 9). The authors concluded that their results support the hypothesis that, in type 2 diabetes, increased intestinal input of triglyceride can lead to elevated fasting and postprandial plasma triglycerides. triglyceride.

[35697] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35698] Carlsson, M.; Orho-Melander, M.; Hedenbro, J.; Almgren, P.; Groop, L. C. : The T54 allele of the intestinal fatty acid-binding protein 2 is associated with a parental history of stroke. J. Clin. Endocr. Metab. 85: 2801–2804, 2000. ; and

[35699] Georgopoulos, A.; Aras, O.; Tsai, M. Y. : Codon-54 polymorphism of the fatty acid-binding protein 2 gene is associated with elevation of fasting and postprandial triglyceride in type 2.

[35700] Further studies establishing the function and utilities of FABP2 are found in John Hopkins OMIM database record ID 134640, and in cited publications numbered 617–627 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC114971

(Accession XM_054936) is another VGAM951 host target gene. LOC114971 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114971 BINDING SITE, designated SEQ ID:36208, to the nucleotide sequence of VGAM951 RNA, herein designated VGAM RNA, also designated SEQ ID:3662.

[35701] Another function of VGAM951 is therefore inhibition of LOC114971 (Accession XM_054936). Accordingly, utilities of VGAM951 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114971. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 952 (VGAM952) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35702] VGAM952 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM952 was detected is described hereinabove with reference to Figs. 1-8.

[35703] VGAM952 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Bushy Stunt Virus. VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35704] VGAM952 gene encodes a VGAM952 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM952 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM952 precursor RNA is designated SEQ ID:938, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:938 is located at position 3036 relative to the genome of Tomato Bushy Stunt Virus.

[35705] VGAM952 precursor RNA folds onto itself, forming VGAM952 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[35706] An enzyme complex designated DICER COMPLEX, `dices` the VGAM952 folded precursor RNA into VGAM952 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 89%) nucleotide sequence of VGAM952 RNA is designated SEQ ID:3663, and is provided hereinbelow with reference to the sequence listing part.

[35707] VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM952 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35708] VGAM952 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM952 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM952 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM952 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35709] The complementary binding of VGAM952 RNA, herein designated VGAM RNA, to host target binding sites on VGAM952 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM952 host target RNA into VGAM952 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35710] It is appreciated that VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM952 host target genes. The mRNA of each one of this plurality of VGAM952 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM952 RNA, herein designated VGAM RNA, and which when bound by VGAM952 RNA causes inhibition of translation of respective one or more VGAM952 host target proteins.

[35711] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM952 gene, herein designated VGAM GENE, on one or more VGAM952 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35712] It is yet further appreciated that a function of VGAM952 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of viral infection by Tomato Bushy Stunt Virus. Specific functions, and accordingly utilities, of VGAM952 correlate with, and may be deduced from, the identity of the host target genes which VGAM952 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35713] Nucleotide sequences of the VGAM952 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM952 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM952 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM952 are further described hereinbelow with reference to Table 1.

[35714] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM952 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM952 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35715] As mentioned hereinabove with reference to Fig. 1, a function of VGAM952 gene, herein designated VGAM is inhibition of expression of VGAM952 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM952 correlate with, and may be deduced from, the identity of the target genes which VGAM952 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35716] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778) is a VGAM952 host target gene. B4GALT4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT4 BINDING SITE, designated SEQ ID:9862, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35717] A function of VGAM952 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT4. Cyclin T2 (CCNT2, Accession NM_058241) is another VGAM952 host target gene. CCNT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNT2 BINDING SITE, designated SEQ ID:27771, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35718] Another function of VGAM952 is therefore inhibition of Cyclin T2 (CCNT2, Accession NM_058241), a gene which is a regulatory subunit of the cyclin-dependent kinase

pair (cdk9/cyclin t) complex. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNT2. The function of CCNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM159. Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is another VGAM952 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14890, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35719] Another function of VGAM952 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499) is another VGAM952 host target gene. NEO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEO1 BINDING SITE, designated SEQ ID:8321, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35720] Another function of VGAM952 is therefore inhibition of Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499), a gene which regulates the transition of undifferentiated proliferating cells to their differentiated state. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEO1. The function of NEO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM329. Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM_013261) is another VGAM952 host target gene. PPARGC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPARGC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPARGC1 BINDING SITE, designated SEQ ID:14934, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35721] Another function of VGAM952 is therefore inhibition of Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1 (PPARGC1, Accession NM_013261), a gene which may play a role in insulin sensitivity and thermogenesis. Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPARGC1. The function of PPARGC1 has been established by previous studies. Adaptive thermogenesis is an important component of energy homeostasis and a metabolic defense against obesity, which is characterized by a chronic imbalance between

energy intake and expenditure. Part of energy expenditure results from a leaking of protons across the mitochondrial inner membrane which leads to energy dissipation because of uncoupling of oxygen consumption to ATP synthesis. Three mitochondrial uncoupling proteins, UCP1 (OMIM Ref. No. 113730), UCP2 (OMIM Ref. No. 601693), and UCP3 (OMIM Ref. No. 602044), are candidates to explain the proton leak. The most compelling evidence for a direct role of uncoupling proteins in the proton leak comes from data on brown fat-specific UCP1. During cold exposure, energy dissipation is increased through brown adipose tissue (BAT) hypertrophy, biogenesis of mitochondria, and increased expression and activation of UCP1. Data pointed to peroxisome proliferator-activated receptor-gamma (PPARG; 601487) as a transcriptional regulator of uncoupling protein expression. PPAR-gamma is a nuclear receptor activated by fatty acids and eicosanoids which plays a major role in adipocyte differentiation. In brown fat cells, PPARG activates an enhancer of the UCP1 gene promoter. Puigserver et al. (1998) cloned a novel transcription coactivator of nuclear receptors, termed Pgc1, from a mouse brown fat cDNA library. Pgc1 mRNA expression was dramatically elevated upon

cold exposure of mice in both brown fat and skeletal muscle, key thermogenic tissues. Pgc1 greatly increased the transcriptional activity of Ppar-gamma (OMIM Ref. No. 601487) and thyroid hormone receptor (see OMIM Ref. No. 190120) on the uncoupling protein Ucp1 (OMIM Ref. No. 113730) promoter. Ectopic expression of Pgc1 in white adipose cells activated expression of Ucp1 and key mitochondrial enzymes of the respiratory chain, and increased the cellular content of mitochondrial DNA.

Puigserver et al. (1998) suggested that PGC1 plays a key role in linking nuclear receptors to the transcriptional program of adaptive thermogenesis. Animal model experiments lend further support to the function of PPARGC1. Herzig et al. (2001) demonstrated that mice carrying a targeted disruption of the cAMP response element-binding (CREB) protein gene (OMIM Ref. No. 123810), or overexpressing a dominant-negative CREB inhibitor, exhibit fasting hyperglycemia and reduced expression of gluconeogenic enzymes. CREB was found to induce expression of the gluconeogenic program through the nuclear receptor coactivator PGC1, which was demonstrated to be a direct target for CREB regulation in vivo. Overexpression of PGC1 in CREB-deficient mice restored glucose homeosta-

sis and rescued the expression of gluconeogenic genes. In transient assays, PGC1 potentiated glucocorticoid induction of the gene for PEPCK, the rate-limiting enzyme in gluconeogenesis. PGC1 promotes cooperativity between cAMP and glucocorticoid signaling pathways during hepatic gluconeogenesis. Fasting hyperglycemia is strongly correlated with type II diabetes (OMIM Ref. No. 125853), so Herzig et al. (2001) concluded that the activation of PGC1 by CREB in liver contributes importantly to the pathogenesis of this disease.

[35722] It is appreciated that the abovementioned animal model for PPARGC1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[35723] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35724] Puigserver, P.; Wu, Z.; Park, C. W.; Graves, R.; Wright, M.; Spiegelman, B. M. : A cold-inducible coactivator of nuclear receptors linked to adaptive thermogenesis. Cell 92: 829–839, 1998. ; and

[35725] Herzig, S.; Long, F.; Jhala, U. S.; Hedrick, S.; Quinn, R.; Bauer, A.; Rudolph, D.; Schutz, G.; Yoon, C.; Puigserver, P.;

Spiegelman, B.; Montminy, M. : CREB regulates hepatic gluconeogenesis.

[35726] Further studies establishing the function and utilities of PPARGC1 are found in John Hopkins OMIM database record ID 604517, and in cited publications numbered 4789, 490 and 11857–6932 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 21 Open Reading Frame 100 (C21orf100, Accession NM_145033) is another VGAM952 host target gene. C21orf100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf100 BINDING SITE, designated SEQ ID:29650, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35727] Another function of VGAM952 is therefore inhibition of Chromosome 21 Open Reading Frame 100 (C21orf100, Accession NM_145033). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf100. DK–

FZP434N178 (Accession XM_050278) is another VGAM952 host target gene. DKFZP434N178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434N178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N178 BINDING SITE, designated SEQ ID:35600, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35728] Another function of VGAM952 is therefore inhibition of DKFZP434N178 (Accession XM_050278). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N178. Down Syndrome Critical Region Gene 6 (DSCR6, Accession NM_018962) is another VGAM952 host target gene. DSCR6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR6 BINDING SITE, designated SEQ ID:21031, to the nucleotide sequence of

VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35729] Another function of VGAM952 is therefore inhibition of Down Syndrome Critical Region Gene 6 (DSCR6, Accession NM_018962). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR6. FACTP140 (Accession NM_007192) is another VGAM952 host target gene. FACTP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FACTP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACTP140 BINDING SITE, designated SEQ ID:14046, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35730] Another function of VGAM952 is therefore inhibition of FACTP140 (Accession NM_007192). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACTP140. FLJ23360 (Accession NM_023076) is another VGAM952 host target gene. FLJ23360 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23360 BINDING SITE, designated SEQ ID:23338, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35731] Another function of VGAM952 is therefore inhibition of FLJ23360 (Accession NM_023076). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23360. HSA250839 (Accession NM_018401) is another VGAM952 host target gene. HSA250839 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA250839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA250839 BINDING SITE, designated SEQ ID:20440, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35732] Another function of VGAM952 is therefore inhibition of

HSA250839 (Accession NM_018401). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA250839. LOC143943 (Accession XM_096504) is another VGAM952 host target gene. LOC143943 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143943 BINDING SITE, designated SEQ ID:40385, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35733] Another function of VGAM952 is therefore inhibition of LOC143943 (Accession XM_096504). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143943. LOC151610 (Accession XM_087245) is another VGAM952 host target gene. LOC151610 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC151610 BINDING SITE, designated SEQ ID:39139, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35734] Another function of VGAM952 is therefore inhibition of LOC151610 (Accession XM_087245). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151610. LOC200609 (Accession XM_117256) is another VGAM952 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43339, to the nucleotide sequence of VGAM952 RNA, herein designated VGAM RNA, also designated SEQ ID:3663.

[35735] Another function of VGAM952 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM952 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 953 (VGAM953) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35736] VGAM953 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM953 was detected is described hereinabove with reference to Figs. 1–8.

[35737] VGAM953 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35738] VGAM953 gene encodes a VGAM953 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM953 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM953 precursor RNA is designated SEQ ID:939, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:939 is

located at position 3700 relative to the genome of Tomato Spotted Wilt Virus.

[35739] VGAM953 precursor RNA folds onto itself, forming VGAM953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35740] An enzyme complex designated DICER COMPLEX, `dices` the VGAM953 folded precursor RNA into VGAM953 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM953 RNA is designated SEQ ID:3664, and is provided hereinbelow with reference to the sequence listing part.

[35741] VGAM953 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM953 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[35742] VGAM953 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM953 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM953 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM953 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35743] The complementary binding of VGAM953 RNA, herein designated VGAM RNA, to host target binding sites on VGAM953 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM953 host target RNA into VGAM953 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35744] It is appreciated that VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM953 host target genes. The mRNA of each one of this plurality of VGAM953 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM953 RNA, herein designated VGAM RNA, and which when bound by VGAM953 RNA causes inhibition of translation of respective one or more VGAM953

host target proteins.

[35745] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM953 gene, herein designated VGAM GENE, on one or more VGAM953 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35746] It is yet further appreciated that a function of VGAM953 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus.

Specific functions, and accordingly utilities, of VGAM953 correlate with, and may be deduced from, the identity of the host target genes which VGAM953 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35747] Nucleotide sequences of the VGAM953 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM953 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM953 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM953 are further described hereinbelow with reference to Table 1.

[35748] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM953 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM953 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35749] As mentioned hereinabove with reference to Fig. 1, a function of VGAM953 gene, herein designated VGAM is inhibition of expression of VGAM953 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM953 correlate with, and may be deduced from, the identity of the target genes which VGAM953 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35750] EH-domain Containing 4 (EHD4, Accession NM_139265) is a VGAM953 host target gene. EHD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EHD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD4 BINDING SITE, designated SEQ ID:29256, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35751] A function of VGAM953 is therefore inhibition of EH-domain Containing 4 (EHD4, Accession NM_139265). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD4. Exostoses (multiple)-like 2 (EXTL2, Accession NM_001439) is another VGAM953 host target gene. EXTL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL2 BINDING SITE, designated SEQ ID:7160, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35752] Another function of VGAM953 is therefore inhibition of Exostoses (multiple)-like 2 (EXTL2, Accession NM_001439), a gene which is homologous to the EXT and EXTL genes. Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL2. The function of EXTL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM743. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275) is another VGAM953 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14603,

to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35753] Another function of VGAM953 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263.S100 Calcium Binding Protein A5 (S100A5, Accession NM_002962) is another VGAM953 host target gene. S100A5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by S100A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of S100A5 BINDING SITE, designated SEQ ID:8876, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35754] Another function of VGAM953 is therefore inhibition of

S100 Calcium Binding Protein A5 (S100A5, Accession NM_002962), a gene which interacts with target proteins to link extracellular stimuli and cellular responses; member of the S100 family of tissue-specific calcium-binding proteins. Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with S100A5. The function of S100A5 has been established by previous studies. The S100 proteins are small calcium-binding proteins which display different expression patterns in human tissues. Some S100 proteins are associated with tumor development and the metastatic behavior of tumors. Engelkamp et al. (1993) established the physical linkage of 6 S100 genes by pulsed field gel electrophoresis and DNA sequencing of 15 kb containing the full coding region of 4 different S100 genes: S100E (S100A3; 176992), CAPL (S100A4; 114210), S100D (OMIM Ref. No. S100A5), and calcyclin (S100A6; 114110). Engelkamp et al. (1993) stated that 'this is the tightest mammalian gene cluster discovered so far.' The cluster was assigned to 1q21 by in situ hybridization. Two other S100 genes were located within 450 kb: S100L (S100A2; 176993) and S100A (S100A1; 176940). Schafer et al. (1995) isolated a YAC

from 1q21 on which 9 different genes coding for S100 calcium-binding proteins could be localized. The clustered organization of S100 genes allowed introduction of a new logical nomenclature based on their physical arrangement on the chromosome, with S100A1 being closest to the telomere and S100A9 (OMIM Ref. No. 123886) being closest to the centromere. In this nomenclature, S100D became S100A5.

[35755] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35756] Engelkamp, D.; Schafer, B. W.; Mattei, M. G.; Erne, P.; Heizmann, C. W. : Six S100 genes are clustered on human chromosome 1q21: identification of two genes coding for the two previously unreported calcium-binding proteins S100D and S100E. Proc. Nat. Acad. Sci. 90: 6547–6551, 1993. ; and

[35757] Schafer, B. W.; Wicki, R.; Engelkamp, D.; Mattei, M.–G.; Heizmann, C. W. : Isolation of a YAC clone covering a cluster of nine S100 genes on human chromosome 1q21: rationale for a new no.

[35758] Further studies establishing the function and utilities of S100A5 are found in John Hopkins OMIM database record

ID 176991, and in cited publications numbered 12359 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 12 Open Reading Frame 2 (C12orf2, Accession XM_096040) is another VGAM953 host target gene. C12orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C12orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C12orf2 BINDING SITE, designated SEQ ID:40290, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35759] Another function of VGAM953 is therefore inhibition of Chromosome 12 Open Reading Frame 2 (C12orf2, Accession XM_096040). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C12orf2. Chromosome 20 Open Reading Frame 38 (C20orf38, Accession NM_018327) is another VGAM953 host target gene. C20orf38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf38, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf38 BINDING SITE, designated SEQ ID:20323, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35760] Another function of VGAM953 is therefore inhibition of Chromosome 20 Open Reading Frame 38 (C20orf38, Accession NM_018327). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf38. C6orf5 (Accession NM_015524) is another VGAM953 host target gene. C6orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf5 BINDING SITE, designated SEQ ID:17779, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35761] Another function of VGAM953 is therefore inhibition of C6orf5 (Accession NM_015524). Accordingly, utilities of

VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf5. Cartilage Acidic Protein 1 (CRTAC1, Accession NM_018058) is another VGAM953 host target gene. CRTAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRTAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRTAC1 BINDING SITE, designated SEQ ID:19827, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35762] Another function of VGAM953 is therefore inhibition of Cartilage Acidic Protein 1 (CRTAC1, Accession NM_018058). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRTAC1. DKFZp547A023 (Accession XM_052065) is another VGAM953 host target gene. DKFZp547A023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547A023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547A023 BINDING SITE, designated SEQ ID:35940, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35763] Another function of VGAM953 is therefore inhibition of DKFZp547A023 (Accession XM_052065). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547A023. FLJ10314 (Accession NM_018055) is another VGAM953 host target gene. FLJ10314 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10314, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10314 BINDING SITE, designated SEQ ID:19815, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35764] Another function of VGAM953 is therefore inhibition of FLJ10314 (Accession NM_018055). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10314.

G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776) is another VGAM953 host target gene. GIT2 BINDING SITE1 through GIT2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GIT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE1 through GIT2 BINDING SITE3, designated SEQ ID:16604, SEQ ID:27686 and SEQ ID:27699 respectively, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35765] Another function of VGAM953 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM953 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12801, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35766] Another function of VGAM953 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. MGC30052 (Accession NM_144721) is another VGAM953 host target gene. MGC30052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC30052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC30052 BINDING SITE, designated SEQ ID:29543, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35767] Another function of VGAM953 is therefore inhibition of MGC30052 (Accession NM_144721). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC30052. LOC149386 (Accession XM_097631) is another VGAM953 host target gene. LOC149386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149386 BINDING SITE, designated SEQ ID:40985, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35768] Another function of VGAM953 is therefore inhibition of LOC149386 (Accession XM_097631). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149386. LOC154789 (Accession XM_088043) is another VGAM953 host target gene. LOC154789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154789 BINDING SITE, designated SEQ ID:39487, to the nucleotide sequence of VGAM953 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3664.

[35769] Another function of VGAM953 is therefore inhibition of LOC154789 (Accession XM_088043). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154789. LOC158563 (Accession XM_088606) is another VGAM953 host target gene. LOC158563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158563 BINDING SITE, designated SEQ ID:39866, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35770] Another function of VGAM953 is therefore inhibition of LOC158563 (Accession XM_088606). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158563. LOC255270 (Accession XM_170578) is another VGAM953 host target gene. LOC255270 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255270, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255270 BINDING SITE, designated SEQ ID:45389, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35771] Another function of VGAM953 is therefore inhibition of LOC255270 (Accession XM_170578). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255270. LOC51026 (Accession NM_016072) is another VGAM953 host target gene. LOC51026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51026 BINDING SITE, designated SEQ ID:18142, to the nucleotide sequence of VGAM953 RNA, herein designated VGAM RNA, also designated SEQ ID:3664.

[35772] Another function of VGAM953 is therefore inhibition of LOC51026 (Accession NM_016072). Accordingly, utilities of VGAM953 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC51026. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 954 (VGAM954) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35773] VGAM954 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM954 was detected is described hereinabove with reference to Figs. 1–8.

[35774] VGAM954 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35775] VGAM954 gene encodes a VGAM954 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM954 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM954 precursor RNA is designated SEQ

ID:940, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:940 is located at position 4634 relative to the genome of Tomato Spotted Wilt Virus.

[35776] VGAM954 precursor RNA folds onto itself, forming VGAM954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35777] An enzyme complex designated DICER COMPLEX, `dices` the VGAM954 folded precursor RNA into VGAM954 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM954 RNA is designated SEQ ID:3665, and is provided hereinbelow with reference to the sequence

listing part.

[35778] VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM954 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35779] VGAM954 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM954 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM954 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35780] The complementary binding of VGAM954 RNA, herein designated VGAM RNA, to host target binding sites on VGAM954 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM954 host target RNA into VGAM954 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35781] It is appreciated that VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM954 host target genes. The mRNA of each one of this plurality of VGAM954 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM954 RNA, herein designated VGAM

RNA, and which when bound by VGAM954 RNA causes inhibition of translation of respective one or more VGAM954 host target proteins.

[35782] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM954 gene, herein designated VGAM GENE, on one or more VGAM954 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35783] It is yet further appreciated that a function of VGAM954 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM954 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus. Specific functions, and accordingly utilities, of VGAM954 correlate with, and may be deduced from, the identity of the host target genes which VGAM954 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35784] Nucleotide sequences of the VGAM954 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM954 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM954 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM954 are further described hereinbelow with reference to Table 1.

[35785] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM954 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM954 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35786] As mentioned hereinabove with reference to Fig. 1, a function of VGAM954 gene, herein designated VGAM is

inhibition of expression of VGAM954 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM954 correlate with, and may be deduced from, the identity of the target genes which VGAM954 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35787] Glycine Amidinotransferase (L-arginine:glycine amidinotransferase) (GATM, Accession NM_001482) is a VGAM954 host target gene. GATM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATM BINDING SITE, designated SEQ ID:7225, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35788] A function of VGAM954 is therefore inhibition of Glycine Amidinotransferase (L-arginine:glycine amidinotransferase) (GATM, Accession NM_001482), a gene which glycine amidinotransferase; component of the creatine biosynthetic pathway. Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with GATM. The function of GATM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530) is another VGAM954 host target gene. HIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIF1A BINDING SITE, designated SEQ ID:7264, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35789] Another function of VGAM954 is therefore inhibition of Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530), a gene which is a basic helix-loop-helix transcription factor and mediates transcriptional responses to hypoxia and dioxin-signaling. Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with HIF1A. The function of HIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229.AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM_032852) is another VGAM954 host target gene. AUTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AUTL1 BINDING SITE, designated SEQ ID:26650, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35790] Another function of VGAM954 is therefore inhibition of AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM_032852). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AUTL1. Phorbol-12-myristate-13-acetate-induced Protein 1 (PMAIP1, Accession NM_021127) is another VGAM954 host target gene. PMAIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PMAIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMAIP1 BINDING SITE, designated SEQ ID:22099, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35791] Another function of VGAM954 is therefore inhibition of Phorbol-12-myristate-13-acetate-induced Protein 1 (PMAIP1, Accession NM_021127). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMAIP1. PRO2037 (Accession NM_018616) is another VGAM954 host target gene. PRO2037 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2037, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2037 BINDING SITE, designated SEQ ID:20688, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35792] Another function of VGAM954 is therefore inhibition of

PRO2037 (Accession NM_018616). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2037. LOC149711 (Accession XM_097720) is another VGAM954 host target gene. LOC149711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149711 BINDING SITE, designated SEQ ID:41069, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35793] Another function of VGAM954 is therefore inhibition of LOC149711 (Accession XM_097720). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149711. LOC158156 (Accession XM_088496) is another VGAM954 host target gene. LOC158156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158156 BINDING SITE, designated SEQ ID:39737, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35794] Another function of VGAM954 is therefore inhibition of LOC158156 (Accession XM_088496). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158156. LOC162137 (Accession XM_102426) is another VGAM954 host target gene. LOC162137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC162137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162137 BINDING SITE, designated SEQ ID:42116, to the nucleotide sequence of VGAM954 RNA, herein designated VGAM RNA, also designated SEQ ID:3665.

[35795] Another function of VGAM954 is therefore inhibition of LOC162137 (Accession XM_102426). Accordingly, utilities of VGAM954 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162137. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 955 (VGAM955) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35796] VGAM955 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM955 was detected is described hereinabove with reference to Figs. 1–8.

[35797] VGAM955 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35798] VGAM955 gene encodes a VGAM955 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM955 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM955 precursor RNA is designated SEQ ID:941, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:941 is

located at position 4126 relative to the genome of Tomato Spotted Wilt Virus.

[35799] VGAM955 precursor RNA folds onto itself, forming VGAM955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35800] An enzyme complex designated DICER COMPLEX, `dices` the VGAM955 folded precursor RNA into VGAM955 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM955 RNA is designated SEQ ID:3666, and is provided hereinbelow with reference to the sequence listing part.

[35801] VGAM955 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM955 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[35802] VGAM955 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM955 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM955 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM955 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[35803] The complementary binding of VGAM955 RNA, herein designated VGAM RNA, to host target binding sites on VGAM955 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM955 host target RNA into VGAM955 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35804] It is appreciated that VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM955 host target genes. The mRNA of each one of this plurality of VGAM955 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM955 RNA, herein designated VGAM RNA, and which when bound by VGAM955 RNA causes inhibition of translation of respective one or more VGAM955

host target proteins.

[35805] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM955 gene, herein designated VGAM GENE, on one or more VGAM955 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35806] It is yet further appreciated that a function of VGAM955 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus.

Specific functions, and accordingly utilities, of VGAM955 correlate with, and may be deduced from, the identity of the host target genes which VGAM955 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35807] Nucleotide sequences of the VGAM955 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM955 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM955 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM955 are further described hereinbelow with reference to Table 1.

[35808] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM955 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM955 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35809] As mentioned hereinabove with reference to Fig. 1, a function of VGAM955 gene, herein designated VGAM is inhibition of expression of VGAM955 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM955 correlate with, and may be deduced from, the identity of the target genes which VGAM955 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35810] ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028) is a VGAM955 host target gene. ATP11A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11A BINDING SITE, designated SEQ ID:37806, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35811] A function of VGAM955 is therefore inhibition of ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11A. Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812) is another VGAM955 host target gene. BAALC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BAALC, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAALC BINDING SITE, designated SEQ ID:24199, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35812] Another function of VGAM955 is therefore inhibition of Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAALC. Cytochrome P450, Subfamily IIIA (nifedipine oxidase), Polypeptide 4 (CYP3A4, Accession NM_017460) is another VGAM955 host target gene. CYP3A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP3A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP3A4 BINDING SITE, designated SEQ ID:18932, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35813] Another function of VGAM955 is therefore inhibition of

Cytochrome P450, Subfamily IIIA (nifedipine oxidase), Polypeptide 4 (CYP3A4, Accession NM_017460), a gene which may be involved in an nadph-dependent electron transport pathway. Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP3A4. The function of CYP3A4 has been established by previous studies.

Watkins et al. (1985) identified a glucocorticoid-inducible cytochrome P450 in human liver. Molowa et al. (1986) reported the complete cDNA sequence of this P450.

Wrighton and Vandenbranden (1989) isolated a CYP3-type cytochrome P450 from human fetal liver. By somatic cell hybridization and in situ hybridization, Riddell et al.

(1987) assigned to chromosome 7 the gene for a cytochrome P450 that encodes the enzyme nifedipine oxidase (CYP3). The assignment to chromosome 7 was corroborated by Gonzalez et al. (1988) by use of somatic cell hybrids. These authors also provided additional evidence supporting the identity of P450PCN1 and nifedipine oxidase. By multipoint linkage analysis using DNA markers known to be located on chromosome 7, Brooks et al.

(1988) concluded that the most likely location of CYP3 is 7q21-q22.1. No recombination with a COL1A2 (OMIM Ref.

No. 120160) marker was found. Spurr et al. (1989) assigned CYP3 to 7q22-qter by study of a panel of human-rodent somatic cell hybrids. Inoue et al. (1992) mapped CYP3A4 to 7q22.1 by fluorescence in situ hybridization. The induction of CYP3A enzymes is species-specific and believed to involve 1 or more cellular factors, or receptor-like xenosensors. Xie et al. (2000) identified PXR/SXR as one such factor. They showed that targeted disruption of the mouse Pxr gene abolished induction of CYP3A by prototypic inducers such as dexamethasone or pregnenolone-16- α -carbonitrile. In Pxr-null mice carrying a transgene for an activated form of human SXR, there was constitutive upregulation of CYP3A gene expression and enhanced protection against toxic xenobiotic compounds. Xie et al. (2000) demonstrated that species origin of the receptor, rather than the promoter structure of the CYP3A genes, dictates the species-specific pattern of CYP3A inducibility. Thus, they could generate 'humanized' transgenic mice that were responsive to human-specific inducers such as the antibiotic rifampicin. Xie et al. (2000) concluded that the SXR/PXR genes encode the primary species-specific xenosensors that mediate the adaptive hepatic response, and may represent the critical biochem-

ical mechanism of human xenoprotection.

[35814] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35815] Inoue, K.; Inazawa, J.; Nakagawa, H.; Shimada, T.; Yamazaki, H.; Guengerich, F. P.; Abe, T. : Assignment of the human cytochrome P-450 nifedipine oxidase gene (CYP3A4) to chromosome 7 at band q22.1 by fluorescence in situ hybridization. Jpn. J. Hum. Genet. 37: 133-138, 1992. ; and

[35816] Xie, W.; Barwick, J. L.; Downes, M.; Blumberg, B.; Simon, C. M.; Nelson, M. C.; Neuschwander-Tetri, B. A.; Brunt, E. M.; Guzelian, P. S.; Evans, R. M. : Humanized xenobiotic response.

[35817] Further studies establishing the function and utilities of CYP3A4 are found in John Hopkins OMIM database record ID 124010, and in cited publications numbered 3412-3425, 12760-12761, 3426-3428, 366 and 3672-3681 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM_003583) is another VGAM955 host target gene. DYRK2 BINDING SITE1 and

DYRK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2, designated SEQ ID:9631 and SEQ ID:13207 respectively, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35818] Another function of VGAM955 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM_003583). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK2. Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM_016348) is another VGAM955 host target gene. C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C5orf4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4

BINDING SITE1 and C5orf4 BINDING SITE2, designated SEQ ID:18477 and SEQ ID:26186 respectively, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35819] Another function of VGAM955 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM_016348). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. DKFZp434F142 (Accession NM_032254) is another VGAM955 host target gene. DKFZp434F142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F142 BINDING SITE, designated SEQ ID:25996, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35820] Another function of VGAM955 is therefore inhibition of DKFZp434F142 (Accession NM_032254). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp434F142. DKFZP434K1772 (Accession XM_041936) is another VGAM955 host target gene. DKFZP434K1772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434K1772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K1772 BINDING SITE, designated SEQ ID:33632, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35821] Another function of VGAM955 is therefore inhibition of DKFZP434K1772 (Accession XM_041936). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434K1772. Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM_057927) is another VGAM955 host target gene. FHOD2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FHOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHOD2 BINDING

SITE, designated SEQ ID:36551, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35822] Another function of VGAM955 is therefore inhibition of Formin Homology 2 Domain Containing 2 (FHOD2, Accession XM_057927). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHOD2. FLJ14437 (Accession NM_032578) is another VGAM955 host target gene. FLJ14437 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14437 BINDING SITE, designated SEQ ID:26309, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35823] Another function of VGAM955 is therefore inhibition of FLJ14437 (Accession NM_032578). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14437. KIAA0084 (Accession XM_042841) is another VGAM955

host target gene. KIAA0084 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0084 BINDING SITE, designated SEQ ID:33807, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35824] Another function of VGAM955 is therefore inhibition of KIAA0084 (Accession XM_042841). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0084. MGC3130 (Accession NM_024032) is another VGAM955 host target gene. MGC3130 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC3130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3130 BINDING SITE, designated SEQ ID:23462, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35825] Another function of VGAM955 is therefore inhibition of MGC3130 (Accession NM_024032). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3130. PBX/knotted 1 Homeobox 2 (PKNOX2, Accession XM_165574) is another VGAM955 host target gene. PKNOX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKNOX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKNOX2 BINDING SITE, designated SEQ ID:43694, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35826] Another function of VGAM955 is therefore inhibition of PBX/knotted 1 Homeobox 2 (PKNOX2, Accession XM_165574). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKNOX2. SBB103 (Accession NM_005785) is another VGAM955 host target gene. SBB103 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SBB103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBB103 BINDING SITE, designated SEQ ID:12368, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35827] Another function of VGAM955 is therefore inhibition of SBB103 (Accession NM_005785). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBB103. SCOP (Accession XM_166290) is another VGAM955 host target gene. SCOP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCOP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCOP BINDING SITE, designated SEQ ID:44103, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35828] Another function of VGAM955 is therefore inhibition of SCOP (Accession XM_166290). Accordingly, utilities of

VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCOP.

TIP120A (Accession NM_018448) is another VGAM955 host target gene. TIP120A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TIP120A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIP120A BINDING SITE, designated SEQ ID:20517, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35829] Another function of VGAM955 is therefore inhibition of TIP120A (Accession NM_018448). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIP120A. TRIAD3 (Accession XM_170517) is another VGAM955 host target gene. TRIAD3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIAD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIAD3 BINDING SITE, designated

SEQ ID:45349, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35830] Another function of VGAM955 is therefore inhibition of TRIAD3 (Accession XM_170517). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIAD3. Vav 3 Oncogene (VAV3, Accession NM_006113) is another VGAM955 host target gene. VAV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VAV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAV3 BINDING SITE, designated SEQ ID:12759, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35831] Another function of VGAM955 is therefore inhibition of Vav 3 Oncogene (VAV3, Accession NM_006113). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAV3. ZNF361 (Accession NM_018555) is another VGAM955 host target gene. ZNF361 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF361 BINDING SITE, designated SEQ ID:20635, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35832] Another function of VGAM955 is therefore inhibition of ZNF361 (Accession NM_018555). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF361. LOC144161 (Accession XM_096548) is another VGAM955 host target gene. LOC144161 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144161 BINDING SITE, designated SEQ ID:40389, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35833] Another function of VGAM955 is therefore inhibition of

LOC144161 (Accession XM_096548). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144161. LOC150035 (Accession XM_097793) is another VGAM955 host target gene. LOC150035 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150035 BINDING SITE, designated SEQ ID:41121, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35834] Another function of VGAM955 is therefore inhibition of LOC150035 (Accession XM_097793). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150035. LOC151098 (Accession XM_087096) is another VGAM955 host target gene. LOC151098 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC151098 BINDING SITE, designated SEQ ID:39049, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35835] Another function of VGAM955 is therefore inhibition of LOC151098 (Accession XM_087096). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151098. LOC219540 (Accession XM_168047) is another VGAM955 host target gene. LOC219540 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219540 BINDING SITE, designated SEQ ID:44957, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35836] Another function of VGAM955 is therefore inhibition of LOC219540 (Accession XM_168047). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219540. LOC257475 (Accession XM_051670) is an-

other VGAM955 host target gene. LOC257475 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257475 BINDING SITE, designated SEQ ID:35860, to the nucleotide sequence of VGAM955 RNA, herein designated VGAM RNA, also designated SEQ ID:3666.

[35837] Another function of VGAM955 is therefore inhibition of LOC257475 (Accession XM_051670). Accordingly, utilities of VGAM955 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257475. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 956 (VGAM956) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35838] VGAM956 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM956 was detected is described

hereinabove with reference to Figs. 1–8.

[35839] VGAM956 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35840] VGAM956 gene encodes a VGAM956 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM956 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM956 precursor RNA is designated SEQ ID:942, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:942 is located at position 3426 relative to the genome of Tomato Spotted Wilt Virus.

[35841] VGAM956 precursor RNA folds onto itself, forming VGAM956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35842] An enzyme complex designated DICER COMPLEX, `dices` the VGAM956 folded precursor RNA into VGAM956 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM956 RNA is designated SEQ ID:3667, and is provided hereinbelow with reference to the sequence listing part.

[35843] VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM956 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35844] VGAM956 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM956 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM956 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM956 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35845] The complementary binding of VGAM956 RNA, herein designated VGAM RNA, to host target binding sites on VGAM956 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM956 host target RNA into VGAM956 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35846] It is appreciated that VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM956 host target genes. The mRNA of each one of this plurality of VGAM956 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM956 RNA, herein designated VGAM RNA, and which when bound by VGAM956 RNA causes inhibition of translation of respective one or more VGAM956 host target proteins.

[35847] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM956 gene, herein designated VGAM GENE, on one or more VGAM956 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35848] It is yet further appreciated that a function of VGAM956 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus. Specific functions, and accordingly utilities, of VGAM956 correlate with, and may be deduced from, the identity of the host target genes which VGAM956 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35849] Nucleotide sequences of the VGAM956 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM956 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM956 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM956 are further described hereinbelow with reference to Table 1.

[35850] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM956 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM956 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35851] As mentioned hereinabove with reference to Fig. 1, a function of VGAM956 gene, herein designated VGAM is inhibition of expression of VGAM956 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM956 correlate with, and may be deduced from, the identity of the target genes which VGAM956 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35852] JJAZ1 (Accession NM_015355) is a VGAM956 host target gene. JJAZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JJAZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of JJAZ1 BINDING SITE, designated SEQ ID:17656, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35853] A function of VGAM956 is therefore inhibition of JJAZ1 (Accession NM_015355), a gene which is a zinc finger protein. Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JJAZ1. The function of JJAZ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM231. NEBL (Accession NM_006393) is another VGAM956 host target gene. NEBL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEBL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEBL BINDING SITE, designated SEQ ID:13099, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35854] Another function of VGAM956 is therefore inhibition of NEBL (Accession NM_006393). Accordingly, utilities of

VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEBL.

TEM7 (Accession NM_020405) is another VGAM956 host target gene. TEM7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM7 BINDING SITE, designated SEQ ID:21671, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35855] Another function of VGAM956 is therefore inhibition of TEM7 (Accession NM_020405), a gene which involves in angiogenesis. Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM7. The function of TEM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM23.FLJ11274 (Accession NM_018375) is another VGAM956 host target gene. FLJ11274 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ11274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11274 BINDING SITE, designated SEQ ID:20397, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35856] Another function of VGAM956 is therefore inhibition of FLJ11274 (Accession NM_018375). Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11274. MGC12981 (Accession NM_032357) is another VGAM956 host target gene. MGC12981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12981 BINDING SITE, designated SEQ ID:26142, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35857] Another function of VGAM956 is therefore inhibition of MGC12981 (Accession NM_032357). Accordingly, utilities

of VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12981. LOC143310 (Accession XM_084485) is another VGAM956 host target gene. LOC143310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143310 BINDING SITE, designated SEQ ID:37610, to the nucleotide sequence of VGAM956 RNA, herein designated VGAM RNA, also designated SEQ ID:3667.

[35858] Another function of VGAM956 is therefore inhibition of LOC143310 (Accession XM_084485). Accordingly, utilities of VGAM956 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143310. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 957 (VGAM957) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35859] VGAM957 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM957 was detected is described hereinabove with reference to Figs. 1–8.

[35860] VGAM957 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35861] VGAM957 gene encodes a VGAM957 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM957 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM957 precursor RNA is designated SEQ ID:943, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:943 is located at position 704 relative to the genome of Tomato Spotted Wilt Virus.

[35862] VGAM957 precursor RNA folds onto itself, forming VGAM957 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35863] An enzyme complex designated DICER COMPLEX, `dices` the VGAM957 folded precursor RNA into VGAM957 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM957 RNA is designated SEQ ID:3668, and is provided hereinbelow with reference to the sequence listing part.

[35864] VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM957 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[35865] VGAM957 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM957 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM957 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35866] The complementary binding of VGAM957 RNA, herein designated VGAM RNA, to host target binding sites on VGAM957 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM957 host target RNA into VGAM957 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35867] It is appreciated that VGAM957 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM957 host target genes. The mRNA of each one of this plurality of VGAM957 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM957 RNA, herein designated VGAM RNA, and which when bound by VGAM957 RNA causes inhibition of translation of respective one or more VGAM957 host target proteins.

[35868] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM957 gene, herein designated VGAM GENE, on one or more VGAM957 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35869] It is yet further appreciated that a function of VGAM957 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus. Specific functions, and accordingly utilities, of VGAM957 correlate with, and may be deduced from, the identity of the host target genes which VGAM957 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35870] Nucleotide sequences of the VGAM957 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM957 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM957 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM957 are further
described hereinbelow with reference to Table 1.

[35871] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM957 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM957 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[35872] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM957 gene, herein designated VGAM is
inhibition of expression of VGAM957 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM957 correlate with, and may be deduced
from, the identity of the target genes which VGAM957
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[35873] Golgi Autoantigen, Golgin Subfamily A, 4 (GOLGA4, Ac-
cession XM_011069) is a VGAM957 host target gene.

GOLGA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLGA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA4 BINDING SITE, designated SEQ ID:30165, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35874] A function of VGAM957 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 4 (GOLGA4, Accession XM_011069), a gene which may play a role in vesicular transport from the trans- golgi. Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA4. The function of GOLGA4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM841. Outer Dense Fiber of Sperm Tails 2 (ODF2, Accession NM_002540) is another VGAM957 host target gene. ODF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ODF2, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ODF2 BINDING SITE, designated SEQ ID:8389, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35875] Another function of VGAM957 is therefore inhibition of Outer Dense Fiber of Sperm Tails 2 (ODF2, Accession NM_002540), a gene which is very strongly similar to rat Odf2 . Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ODF2. The function of ODF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM363. Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430) is another VGAM957 host target gene. PAFAH1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAFAH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAFAH1B1 BINDING SITE, designated SEQ

ID:6015, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35876] Another function of VGAM957 is therefore inhibition of Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAFAH1B1. Steroid-5-alpha-reductase, Alpha Polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2) (SRD5A2, Accession XM_002471) is another VGAM957 host target gene. SRD5A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SRD5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRD5A2 BINDING SITE, designated SEQ ID:29888, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35877] Another function of VGAM957 is therefore inhibition of Steroid-5-alpha-reductase, Alpha Polypeptide 2 (3-oxo-5

alpha-steroid delta 4-dehydrogenase alpha 2) (SRD5A2, Accession XM_002471). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRD5A2. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM957 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15358, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35878] Another function of VGAM957 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM172.Chromosome 20 Open Reading Frame 21 (C20orf21, Accession NM_017798) is another VGAM957 host target gene. C20orf21 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf21 BINDING SITE, designated SEQ ID:19443, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35879] Another function of VGAM957 is therefore inhibition of Chromosome 20 Open Reading Frame 21 (C20orf21, Accession NM_017798). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf21. DKFZP564O0423 (Accession XM_166254) is another VGAM957 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44071, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35880] Another function of VGAM957 is therefore inhibition of DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. FLJ13072 (Accession XM_117117) is another VGAM957 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43238, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35881] Another function of VGAM957 is therefore inhibition of FLJ13072 (Accession XM_117117). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13072. FLJ20055 (Accession NM_017643) is another VGAM957

host target gene. FLJ20055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20055 BINDING SITE, designated SEQ ID:19147, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35882] Another function of VGAM957 is therefore inhibition of FLJ20055 (Accession NM_017643). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20055. MGC14798 (Accession NM_080650) is another VGAM957 host target gene. MGC14798 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC14798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14798 BINDING SITE, designated SEQ ID:27939, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35883] Another function of VGAM957 is therefore inhibition of MGC14798 (Accession NM_080650). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14798. Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM_046751) is another VGAM957 host target gene. PPFIA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPFIA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPFIA4 BINDING SITE, designated SEQ ID:34823, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35884] Another function of VGAM957 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F Polypeptide (PTPRF), Interacting Protein (liprin), Alpha 4 (PPFIA4, Accession XM_046751). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPFIA4. PR Domain Containing 8 (PRDM8, Accession NM_020226) is another

VGAM957 host target gene. PRDM8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRDM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM8 BINDING SITE, designated SEQ ID:21492, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35885] Another function of VGAM957 is therefore inhibition of PR Domain Containing 8 (PRDM8, Accession NM_020226). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM8. LOC129607 (Accession XM_059368) is another VGAM957 host target gene. LOC129607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129607 BINDING SITE, designated SEQ ID:36977, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3668.

[35886] Another function of VGAM957 is therefore inhibition of LOC129607 (Accession XM_059368). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129607. LOC196424 (Accession XM_113718) is another VGAM957 host target gene. LOC196424 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196424, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196424 BINDING SITE, designated SEQ ID:42370, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35887] Another function of VGAM957 is therefore inhibition of LOC196424 (Accession XM_113718). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196424. LOC199692 (Accession NM_145295) is another VGAM957 host target gene. LOC199692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199692, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199692 BINDING SITE, designated SEQ ID:29812, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35888] Another function of VGAM957 is therefore inhibition of LOC199692 (Accession NM_145295). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199692. LOC199848 (Accession XM_117144) is another VGAM957 host target gene. LOC199848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199848 BINDING SITE, designated SEQ ID:43250, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35889] Another function of VGAM957 is therefore inhibition of LOC199848 (Accession XM_117144). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC199848. LOC90841 (Accession XM_034427) is another VGAM957 host target gene. LOC90841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90841 BINDING SITE, designated SEQ ID:32113, to the nucleotide sequence of VGAM957 RNA, herein designated VGAM RNA, also designated SEQ ID:3668.

[35890] Another function of VGAM957 is therefore inhibition of LOC90841 (Accession XM_034427). Accordingly, utilities of VGAM957 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90841. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 958 (VGAM958) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[35891] VGAM958 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM958 was detected is described hereinabove with reference to Figs. 1–8.

[35892] VGAM958 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tomato Spotted Wilt Virus. VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[35893] VGAM958 gene encodes a VGAM958 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM958 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM958 precursor RNA is designated SEQ ID:944, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:944 is located at position 2556 relative to the genome of Tomato Spotted Wilt Virus.

[35894] VGAM958 precursor RNA folds onto itself, forming VGAM958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[35895] An enzyme complex designated DICER COMPLEX, `dices` the VGAM958 folded precursor RNA into VGAM958 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM958 RNA is designated SEQ ID:3669, and is provided hereinbelow with reference to the sequence listing part.

[35896] VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM958 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[35897] VGAM958 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM958 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM958 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[35898] The complementary binding of VGAM958 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM958 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM958 host target RNA into VGAM958 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[35899] It is appreciated that VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM958 host target genes. The mRNA of each one of this plurality of VGAM958 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM958 RNA, herein designated VGAM RNA, and which when bound by VGAM958 RNA causes inhibition of translation of respective one or more VGAM958 host target proteins.

[35900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM958 gene, herein designated VGAM GENE, on one or more VGAM958 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[35901] It is yet further appreciated that a function of VGAM958 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus. Specific functions, and accordingly utilities, of VGAM958 correlate with, and may be deduced from, the identity of the host target genes which VGAM958 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[35902] Nucleotide sequences of the VGAM958 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM958 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM958 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM958 are further described hereinbelow with reference to Table 1.

[35903] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM958 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM958 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[35904] As mentioned hereinabove with reference to Fig. 1, a function of VGAM958 gene, herein designated VGAM is inhibition of expression of VGAM958 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM958 correlate with, and may be deduced from, the identity of the target genes which VGAM958 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[35905] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM_004776) is a VGAM958 host target gene. B4GALT5 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT5 BINDING SITE, designated SEQ ID:11172, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35906] A function of VGAM958 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM_004776). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT5. Basigin (OK blood group) (BSG, Accession NM_001728) is another VGAM958 host target gene. BSG BINDING SITE1 and BSG BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BSG, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BSG BINDING SITE1 and BSG BINDING SITE2, designated SEQ ID:7458 and SEQ ID:33669 respectively, to the nucleotide sequence of VGAM958 RNA,

herein designated VGAM RNA, also designated SEQ ID:3669.

[35907] Another function of VGAM958 is therefore inhibition of Basigin (OK blood group) (BSG, Accession NM_001728), a gene which is a LEUKOCYTE ACTIVATION ANTIGEN and a member of the immunoglobulin superfamily. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BSG. The function of BSG has been established by previous studies. Basigin is a member of the immunoglobulin superfamily, with a structure related to the putative primordial form of the family. It was cloned as a carrier of an oncodevelopmental carbohydrate marker expressed in teratocarcinoma stem cells. It is expressed broadly in both embryos and adults (4,5:Miyauchi et al., 1990, 1991; Kanekura et al., 1991). As members of the immunoglobulin superfamily play fundamental roles in intercellular recognition involved in various immunologic phenomena, differentiation, and development, basigin is thought also to play a role in intercellular recognition. Animal model experiments lend further support to the function of BSG. Naruhashi et al. (1997) generated mice deficient in basigin by targeted disruption. Bsg ^{-/-} mice

showed worse performance than their wildtype and heterozygous littermates in the Y-maze task, which assesses short-term memory, and in the water-finding task, which examines latent learning, without any motor dysfunction. Moreover, the mutant mice showed less acclimation in the habituation task compared with the wildtype mice. The mutant mice were also more sensitive to electric foot shock. Naruhashi et al. (1997) found these findings consistent with the expression profile of basigin in the central nervous system and suggested that basigin may play an important role in learning and memory as well as in sensory functions

[35908] It is appreciated that the abovementioned animal model for BSG is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[35909] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35910] Kanekura, T.; Miyauchi, T.; Tashiro, M.; Muramatsu, T. : Basigin, a new member of the immunoglobulin superfamily: genes in different mammalian species, glycosylation changes in the molecule from adult organs and possible

variation in the N-terminal sequences. Cell Struct. Funct. 16: 23–30, 1991. ; and

[35911] Naruhashi, K.; Kadomatsu, K.; Igakura, T.; Fan, Q.-W.; Kuno, N.; Muramatsu, H.; Miyauchi, T.; Hasegawa, T.; Itoh, A.; Muramatsu, T.; Nabeshima, T. : Abnormalities of sensory and memor.

[35912] Further studies establishing the function and utilities of BSG are found in John Hopkins OMIM database record ID 109480, and in cited publications numbered 21–2 and 1711 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dystrophia Myotonica–protein Kinase (DMPK, Accession NM_004409) is another VGAM958 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10665, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35913] Another function of VGAM958 is therefore inhibition of Dystrophia Myotonica–protein Kinase (DMPK, Accession

NM_004409). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. DXYS155E (Accession NM_005088) is another VGAM958 host target gene. DXYS155E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DXYS155E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXYS155E BINDING SITE, designated SEQ ID:11544, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35914] Another function of VGAM958 is therefore inhibition of DXYS155E (Accession NM_005088), a gene which may be involved in b-cell activation. may also be involved in signal transduction and gene regulation. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DXYS155E. The function of DXYS155E and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766.Erythropoietin (EPO, Accession

NM_000799) is another VGAM958 host target gene. EPO BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EPO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPO BINDING SITE, designated SEQ ID:6468, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35915] Another function of VGAM958 is therefore inhibition of Erythropoietin (EPO, Accession NM_000799). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPO. GA Binding Protein Transcription Factor, Beta Subunit 1, 53kDa (GABPB1, Accession NM_005254) is another VGAM958 host target gene. GABPB1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GABPB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABPB1 BINDING SITE, designated SEQ ID:11761, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM

RNA, also designated SEQ ID:3669.

[35916] Another function of VGAM958 is therefore inhibition of GA Binding Protein Transcription Factor, Beta Subunit 1, 53kDa (GABPB1, Accession NM_005254), a gene which activates adenovirus E4 gene transcription. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABPB1. The function of GABPB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463) is another VGAM958 host target gene. HNRPDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11949, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35917] Another function of VGAM958 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like

(HNRPDL, Accession NM_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Lactate Dehydrogenase B (LDHB, Accession NM_002300) is another VGAM958 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8090, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35918] Another function of VGAM958 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. Mannosidase, Alpha, Class 2C, Member 1 (MAN2C1, Accession XM_053585) is another VGAM958 host target gene. MAN2C1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAN2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN2C1 BINDING SITE, designated SEQ ID:36103, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35919] Another function of VGAM958 is therefore inhibition of Mannosidase, Alpha, Class 2C, Member 1 (MAN2C1, Accession XM_053585), a gene which is Strongly similar to a region of rat ER alpha-mannosidase. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN2C1. The function of MAN2C1 has been established by previous studies. Cytoplasmic alpha-mannosidase (MANA) was assigned to 15q11-qter by study of an X;15

translocation in man–mouse hybrids (Champion et al., 1978). Lysosomal alpha–mannosidase (MANB) has been assigned to chromosome 19 by somatic cell hybridization (see OMIM Ref. No. 248500). Neri et al. (1983) described a boy with a ring chromosome 15 derived from a t(15q;15q) chromosome of the mother. The ring chromosome was duplicated for a portion of the long arms near the centromere, probably cen–q13. Dosage effects suggested that the alpha–mannosidase gene is located in this segment. Since a shortest region of overlap (SRO) of 15q11–qter had been estimated by Ferguson–Smith and Westerveld (1979), the new information places the MAN2C1 gene in the 15q11–q13 segment.

[35920] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35921] Ferguson–Smith, M. A.; Westerveld, A. : Report of the committee on the genetic constitution of chromosomes 13, 14, 15, 16, 17, 18, 19, 20, 21, and 22 (HGM5). Cytogenet. Cell Genet. 25: 59–73, 1979. ; and

[35922] Neri, G.; Ricci, R.; Pelino, A.; Bova, R.; Tedeschi, B.; Serra, A. : A boy with ring chromosome 15 derived from a t(15q;15q) Robertsonian translocation in the mother: cy–

togenetic and bio.

[35923] Further studies establishing the function and utilities of MAN2C1 are found in John Hopkins OMIM database record ID 154580, and in cited publications numbered 11523–11525 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540) is another VGAM958 host target gene. MAT1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAT1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT1A BINDING SITE, designated SEQ ID:43670, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35924] Another function of VGAM958 is therefore inhibition of Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT1A. Metallothionein-like 5, Testis-specific (tesmin) (MTL5, Accession

NM_004923) is another VGAM958 host target gene. MTL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTL5 BINDING SITE, designated SEQ ID:11360, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35925] Another function of VGAM958 is therefore inhibition of Metallothionein-like 5, Testis-specific (tesmin) (MTL5, Accession NM_004923), a gene which functions in metal homeostasis and protects against heavy-metal toxicity. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTL5. The function of MTL5 has been established by previous studies. By randomized RT-PCR on mRNA from mouse tissues, Sugihara et al. (1999) isolated a testis-specific transcript, which they called TF1. By screening a human testis cDNA library with TF1 as a probe, they cloned a novel cDNA, which they called testis-specific metallothionein-like protein, or tesmin. Tesmin encodes a predicted cysteine-rich, 295-amino acid pro-

tein that is 76.3% homologous to mouse tesmin. Sequence analysis revealed the presence of 2 metallothionein (MT)–like motifs. MT expression has been observed to be higher in testes than in liver tissue (Salehi–Ashtiani et al., 1993) and to be actively expressed in a developmentally regulated fashion in mouse male germ cells (De et al., 1991). Tesmin shows no homology to other testis–specific genes. In situ hybridization of adult mouse testicular sections showed that expression of tesmin is restricted to spermatocytes. RT–PCR analysis on testicular transcripts from mice showed that expression of tesmin occurs as early as day 8 and coincides with the entry of germ cells in meiosis.

[35926] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35927] De, S. K.; Enders, G. C.; Andrews, G. K. : High levels of metallothionein messenger RNAs in male germ cells of the adult mouse. *Molec. Endocr.* 5: 628–636, 1991. ; and

[35928] Salehi–Ashtiani, K.; Widrow, R. J.; Markert, C. L.; Goldberg, E. : Testis–specific expression of a metallothionein I–driven transgene correlates with undermethylation of the locus in te.

[35929] Further studies establishing the function and utilities of MTL5 are found in John Hopkins OMIM database record ID 604374, and in cited publications numbered 6921–6923 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM_002474) is another VGAM958 host target gene. MYH11 BINDING SITE1 and MYH11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MYH11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH11 BINDING SITE1 and MYH11 BINDING SITE2, designated SEQ ID:8302 and SEQ ID:23144 respectively, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35930] Another function of VGAM958 is therefore inhibition of Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM_002474), a gene which is involved in muscle contraction. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH11. The function of

MYH11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM_005729) is another VGAM958 host target gene. PPIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIF BINDING SITE, designated SEQ ID:12283, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35931] Another function of VGAM958 is therefore inhibition of Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM_005729), a gene which catalyzes the cis to trans isomerization of certain proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIF. The function of PPIF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Protein S

(alpha) (PROS1, Accession XM_113400) is another VGAM958 host target gene. PROS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROS1 BINDING SITE, designated SEQ ID:42257, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35932] Another function of VGAM958 is therefore inhibition of Protein S (alpha) (PROS1, Accession XM_113400). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROS1. Reticulon 3 (RTN3, Accession XM_058207) is another VGAM958 host target gene. RTN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RTN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RTN3 BINDING SITE, designated SEQ ID:36587, to the nucleotide sequence of VGAM958 RNA, herein designated

VGAM RNA, also designated SEQ ID:3669.

[35933] Another function of VGAM958 is therefore inhibition of Reticulon 3 (RTN3, Accession XM_058207), a gene which is a member of the reticulon (neuroendocrine-specific, NSP) family. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTN3. The function of RTN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM596. Secreted and Transmembrane 1 (SECTM1, Accession NM_003004) is another VGAM958 host target gene. SECTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SECTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SECTM1 BINDING SITE, designated SEQ ID:8911, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35934] Another function of VGAM958 is therefore inhibition of Secreted and Transmembrane 1 (SECTM1, Accession NM_003004). Accordingly, utilities of VGAM958 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SECTM1. Spectrin, Beta, Non-erythrocytic 4 (SPTBN4, Accession NM_025213) is another VGAM958 host target gene. SPTBN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTBN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTBN4 BINDING SITE, designated SEQ ID:24885, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35935] Another function of VGAM958 is therefore inhibition of Spectrin, Beta, Non-erythrocytic 4 (SPTBN4, Accession NM_025213), a gene which is critical for the maintenance of plasma membrane shape and lipid asymmetry. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTBN4. The function of SPTBN4 has been established by previous studies. Tse et al. (2001) cloned SPTBN4, which they termed SPTBN3, as well as a splice variant, sigma-5, encoding a 678-amino acid protein. Whole-mount in situ hybridization analysis revealed

Sptbn4 expression that was restricted to forebrain, hind-brain, and developing eye in postcoital day-9.5 mice. Western blot analysis with polyclonal antibodies detected expression of a predominant 72-kD protein, close to the expected size of the sigma-5 variant. Immunofluorescence microscopy demonstrated colocalization of SPTBN4 with PML (OMIM Ref. No. 102578) and with SUMO1 (UBL1; 601912) in the cytoplasm and nucleus. The authors showed that both the N- and C-terminal helical coils of sigma-5 are needed to form nuclear dots and are associated with the nuclear matrix. Tse et al. (2001) proposed that a spectrin-based skeleton may be important for the structure of the nucleus. Spectrins (e.g., SPTA1; 182860) are rod-shaped proteins that are part of the lattice-like cytoskeleton under the erythrocyte membrane. This meshwork is critical for the maintenance of plasma membrane shape and lipid asymmetry, as revealed by mutant spectrins in diseases such as elliptocytosis (see OMIM Ref. No. 182860) and spherocytosis (see OMIM Ref. No. 182870). Although originally identified in erythrocytes, spectrins have also been found in the membranes of intracellular organelles, such as the Golgi, lysosomes, and secretory vesicles. The spectrin molecule is a tetramer

consisting of 2 alpha and 2 beta subunits, in which the N terminus of an alpha subunit is tightly connected with the C terminus of a beta subunit to form a heterodimer. Spectrin repeats contain approximately 106 amino acids. Alpha subunits have 20 spectrin repeats, while beta subunits have 17. Animal model experiments lend further support to the function of SPTBN4. The autosomal recessive mouse mutation 'quivering' (qv), described by Yoon and Les (1957), produces progressive ataxia with hindlimb paralysis, deafness, and tremor. Ear twitch responses (Preyer reflex) to sound are absent in homozygous qv/qv mice, although cochlear morphology seems normal and cochlear potentials recorded at the round window are no different from those of control mice. However, responses from brain stem auditory nuclei show abnormal transmission of auditory information, indicating that in contrast to the many mutations causing deafness originating in the cochlea, deafness in qv is central in origin (Deol et al., 1983; Bock et al., 1983). Parkinson et al. (2001) reported that qv mice carry loss-of-function mutations in the Spnb4 gene that cause alterations in ion channel localization in myelinated nerves. They concluded that this finding provides a rationale for the auditory and motor neu-

ropathies of these mice.

[35936] It is appreciated that the abovementioned animal model for SPTBN4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[35937] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[35938] Parkinson, N. J.; Olsson, C. L.; Hallows, J. L.; McKee-Johnson, J.; Keogh, B. P.; Noben-Trauth, K.; Kujawa, S. G.; Tempel, B. L. : Mutant beta-spectrin 4 causes auditory and motor neuropathies in quivering mice. Nature Genet. 29: 61-65, 2001. ; and

[35939] Tse, W. T.; Tang, J.; Jin, O.; Korsgren, C.; John, K. M.; Kung, A. L.; Gwynn, B.; Peters, L. L.; Lux, S. E. : A new spectrin, beta-IV, has a major truncated isoform that associates with pr.

[35940] Further studies establishing the function and utilities of SPTBN4 are found in John Hopkins OMIM database record ID 606214, and in cited publications numbered 6166-616 and 6730-6171 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TRIP15 (Accession NM_004236) is another VGAM958

host target gene. TRIP15 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP15 BINDING SITE, designated SEQ ID:10433, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35941] Another function of VGAM958 is therefore inhibition of TRIP15 (Accession NM_004236), a gene which is a subunit of the COP9 signalosome complex. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP15. The function of TRIP15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM452. Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926) is another VGAM958 host target gene. ZFP36L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZFP36L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP36L1 BINDING SITE, designated SEQ ID:11366, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35942] Another function of VGAM958 is therefore inhibition of Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926), a gene which is a regulatory protein involved in regulating the response to growth factors. Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP36L1. The function of ZFP36L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. ADAR3 (Accession NM_018702) is another VGAM958 host target gene.

ADAR3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADAR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAR3 BINDING SITE, designated SEQ ID:20787, to the nucleotide sequence of VGAM958 RNA,

herein designated VGAM RNA, also designated SEQ ID:3669.

[35943] Another function of VGAM958 is therefore inhibition of ADAR3 (Accession NM_018702). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAR3. Apolipoprotein L, 3 (APOL3, Accession NM_014349) is another VGAM958 host target gene. APOL3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by APOL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL3 BINDING SITE, designated SEQ ID:15676, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35944] Another function of VGAM958 is therefore inhibition of Apolipoprotein L, 3 (APOL3, Accession NM_014349). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL3. Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177) is another VGAM958 host target gene. C17orf26 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf26 BINDING SITE, designated SEQ ID:29189, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35945] Another function of VGAM958 is therefore inhibition of Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf26. Chromosome 19 Open Reading Frame 7 (C19orf7, Accession XM_028253) is another VGAM958 host target gene. C19orf7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C19orf7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C19orf7 BINDING SITE, designated SEQ ID:30637, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ

ID:3669.

[35946] Another function of VGAM958 is therefore inhibition of Chromosome 19 Open Reading Frame 7 (C19orf7, Accession XM_028253). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C19orf7. Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM_027172) is another VGAM958 host target gene. C1orf34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf34 BINDING SITE, designated SEQ ID:30441, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35947] Another function of VGAM958 is therefore inhibition of Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM_027172). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf34. Chromosome 20 Open Reading Frame 150 (C20orf150, Accession

XM_037265) is another VGAM958 host target gene.

C20orf150 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf150 BINDING SITE, designated SEQ ID:32598, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35948] Another function of VGAM958 is therefore inhibition of Chromosome 20 Open Reading Frame 150 (C20orf150, Accession XM_037265). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf150. Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM_012264) is another VGAM958 host target gene. C22orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C22orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf5 BINDING SITE, designated SEQ

ID:14583, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35949] Another function of VGAM958 is therefore inhibition of Chromosome 22 Open Reading Frame 5 (C22orf5, Accession NM_012264). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf5. Calsyntenin 2 (CLSTN2, Accession NM_022131) is another VGAM958 host target gene. CLSTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLSTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN2 BINDING SITE, designated SEQ ID:22694, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35950] Another function of VGAM958 is therefore inhibition of Calsyntenin 2 (CLSTN2, Accession NM_022131). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLSTN2. Cyclin M4 (CNNM4, Accession

NM_020184) is another VGAM958 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNNM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM4 BINDING SITE, designated SEQ ID:21428, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35951] Another function of VGAM958 is therefore inhibition of Cyclin M4 (CNNM4, Accession NM_020184). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM4. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295) is another VGAM958 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34945, to the nucleotide sequence of

VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35952] Another function of VGAM958 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665) is another VGAM958 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12217, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35953] Another function of VGAM958 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. FLJ10619 (Accession NM_018156) is another VGAM958 host target gene.

FLJ10619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10619 BINDING SITE, designated SEQ ID:19969, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35954] Another function of VGAM958 is therefore inhibition of FLJ10619 (Accession NM_018156). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10619. FLJ10751 (Accession NM_018205) is another VGAM958 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20096 and SEQ ID:20195 respectively, to the nucleotide sequence of VGAM958 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:3669.

[35955] Another function of VGAM958 is therefore inhibition of FLJ10751 (Accession NM_018205). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. FLJ14642 (Accession NM_032818) is another VGAM958 host target gene. FLJ14642 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14642, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14642 BINDING SITE, designated SEQ ID:26596, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35956] Another function of VGAM958 is therefore inhibition of FLJ14642 (Accession NM_032818). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14642. FLJ20054 (Accession NM_019049) is another VGAM958 host target gene. FLJ20054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20054, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20054 BINDING SITE, designated SEQ ID:21131, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35957] Another function of VGAM958 is therefore inhibition of FLJ20054 (Accession NM_019049). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20054. FLJ20772 (Accession NM_017956) is another VGAM958 host target gene. FLJ20772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20772 BINDING SITE, designated SEQ ID:19667, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35958] Another function of VGAM958 is therefore inhibition of FLJ20772 (Accession NM_017956). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ20772. FLJ21657 (Accession NM_022483) is another VGAM958 host target gene. FLJ21657 BINDING SITE1 and FLJ21657 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ21657, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21657 BINDING SITE1 and FLJ21657 BINDING SITE2, designated SEQ ID:22858 and SEQ ID:22859 respectively, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35959] Another function of VGAM958 is therefore inhibition of FLJ21657 (Accession NM_022483). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21657. H11 (Accession NM_014365) is another VGAM958 host target gene. H11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by H11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H11 BINDING SITE, designated SEQ

ID:15695, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35960] Another function of VGAM958 is therefore inhibition of H11 (Accession NM_014365). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H11. Hyaluronan Binding Protein 2 (HABP2, Accession NM_004132) is another VGAM958 host target gene. HABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HABP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HABP2 BINDING SITE, designated SEQ ID:10345, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35961] Another function of VGAM958 is therefore inhibition of Hyaluronan Binding Protein 2 (HABP2, Accession NM_004132). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HABP2. Integrin, Beta 5

(ITGB5, Accession XM_003029) is another VGAM958 host target gene. ITGB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB5 BINDING SITE, designated SEQ ID:29924, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35962] Another function of VGAM958 is therefore inhibition of Integrin, Beta 5 (ITGB5, Accession XM_003029). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB5. KIAA0040 (Accession NM_014656) is another VGAM958 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16100, to the nucleotide sequence of VGAM958 RNA, herein designated

VGAM RNA, also designated SEQ ID:3669.

[35963] Another function of VGAM958 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. KIAA0205 (Accession NM_014873) is another VGAM958 host target gene. KIAA0205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0205 BINDING SITE, designated SEQ ID:17009, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35964] Another function of VGAM958 is therefore inhibition of KIAA0205 (Accession NM_014873). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0205. KIAA0319 (Accession NM_014809) is another VGAM958 host target gene. KIAA0319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0319, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0319 BINDING SITE, designated SEQ ID:16767, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35965] Another function of VGAM958 is therefore inhibition of KIAA0319 (Accession NM_014809). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0319. KIAA0481 (Accession XM_050144) is another VGAM958 host target gene. KIAA0481 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0481 BINDING SITE, designated SEQ ID:35572, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35966] Another function of VGAM958 is therefore inhibition of KIAA0481 (Accession XM_050144). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0481. KIAA1084 (Accession NM_014910) is another VGAM958 host target gene. KIAA1084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1084 BINDING SITE, designated SEQ ID:17140, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35967] Another function of VGAM958 is therefore inhibition of KIAA1084 (Accession NM_014910). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1084. KIAA1253 (Accession XM_166310) is another VGAM958 host target gene. KIAA1253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1253 BINDING SITE, designated SEQ ID:44133, to the

nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35968] Another function of VGAM958 is therefore inhibition of KIAA1253 (Accession XM_166310). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1253. KIAA1500 (Accession XM_034353) is another VGAM958 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32071, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35969] Another function of VGAM958 is therefore inhibition of KIAA1500 (Accession XM_034353). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. KIAA1673 (Accession XM_047672) is another VGAM958 host target gene. KIAA1673 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1673 BINDING SITE, designated SEQ ID:35027, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35970] Another function of VGAM958 is therefore inhibition of KIAA1673 (Accession XM_047672). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1673. KIAA1719 (Accession XM_042936) is another VGAM958 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33827, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35971] Another function of VGAM958 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities

of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. KIAA1817 (Accession XM_042978) is another VGAM958 host target gene. KIAA1817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1817 BINDING SITE, designated SEQ ID:33864, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35972] Another function of VGAM958 is therefore inhibition of KIAA1817 (Accession XM_042978). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1817. MGC3265 (Accession NM_024028) is another VGAM958 host target gene. MGC3265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3265

BINDING SITE, designated SEQ ID:23458, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35973] Another function of VGAM958 is therefore inhibition of MGC3265 (Accession NM_024028). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3265. MAP Kinase–interacting Serine/threonine Kinase 1 (MKNK1, Accession NM_003684) is another VGAM958 host target gene. MKNK1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MKNK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKNK1 BINDING SITE, designated SEQ ID:9795, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35974] Another function of VGAM958 is therefore inhibition of MAP Kinase–interacting Serine/threonine Kinase 1 (MKNK1, Accession NM_003684). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKNK1.

PRO2955 (Accession NM_018545) is another VGAM958 host target gene. PRO2955 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2955 BINDING SITE, designated SEQ ID:20623, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35975] Another function of VGAM958 is therefore inhibition of PRO2955 (Accession NM_018545). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2955. Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM_024430) is another VGAM958 host target gene. PSTPIP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSTPIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSTPIP2 BINDING SITE, designated SEQ ID:23684, to the nucleotide sequence of

VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35976] Another function of VGAM958 is therefore inhibition of Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM_024430). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSTPIP2. SIMRP7 (Accession XM_166462) is another VGAM958 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44375, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35977] Another function of VGAM958 is therefore inhibition of SIMRP7 (Accession XM_166462). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7. SS-56 (Accession XM_006063) is another VGAM958 host target gene. SS-56 BINDING SITE is HOST TARGET binding

site found in the 5' untranslated region of mRNA encoded by SS-56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS-56 BINDING SITE, designated SEQ ID:29991, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35978] Another function of VGAM958 is therefore inhibition of SS-56 (Accession XM_006063). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS-56. WAC (Accession NM_100264) is another VGAM958 host target gene. WAC BINDING SITE1 through WAC BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WAC, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WAC BINDING SITE1 through WAC BINDING SITE3, designated SEQ ID:28157, SEQ ID:28158 and SEQ ID:18743 respectively, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35979] Another function of VGAM958 is therefore inhibition of WAC (Accession NM_100264). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WAC. LOC115073 (Accession XM_055193) is another VGAM958 host target gene. LOC115073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115073 BINDING SITE, designated SEQ ID:36240, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35980] Another function of VGAM958 is therefore inhibition of LOC115073 (Accession XM_055193). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115073. LOC124460 (Accession XM_071892) is another VGAM958 host target gene. LOC124460 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124460, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124460 BINDING SITE, designated SEQ ID:37447, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35981] Another function of VGAM958 is therefore inhibition of LOC124460 (Accession XM_071892). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124460. LOC125929 (Accession XM_064872) is another VGAM958 host target gene. LOC125929 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC125929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125929 BINDING SITE, designated SEQ ID:37268, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35982] Another function of VGAM958 is therefore inhibition of LOC125929 (Accession XM_064872). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC125929. LOC129011 (Accession XM_059326) is another VGAM958 host target gene. LOC129011 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129011 BINDING SITE, designated SEQ ID:36967, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35983] Another function of VGAM958 is therefore inhibition of LOC129011 (Accession XM_059326). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129011. LOC129138 (Accession NM_138797) is another VGAM958 host target gene. LOC129138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129138 BINDING SITE, designated SEQ ID:29019, to the nucleotide sequence of VGAM958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3669.

[35984] Another function of VGAM958 is therefore inhibition of LOC129138 (Accession NM_138797). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129138. LOC144308 (Accession XM_096575) is another VGAM958 host target gene. LOC144308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144308 BINDING SITE, designated SEQ ID:40408, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35985] Another function of VGAM958 is therefore inhibition of LOC144308 (Accession XM_096575). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144308. LOC144699 (Accession XM_084940) is another VGAM958 host target gene. LOC144699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144699, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144699 BINDING SITE, designated SEQ ID:37771, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35986] Another function of VGAM958 is therefore inhibition of LOC144699 (Accession XM_084940). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144699. LOC145508 (Accession XM_085158) is another VGAM958 host target gene. LOC145508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145508 BINDING SITE, designated SEQ ID:37887, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35987] Another function of VGAM958 is therefore inhibition of LOC145508 (Accession XM_085158). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC145508. LOC146243 (Accession XM_096956) is another VGAM958 host target gene. LOC146243 BINDING SITE1 and LOC146243 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146243, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146243 BINDING SITE1 and LOC146243 BINDING SITE2, designated SEQ ID:40680 and SEQ ID:40681 respectively, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35988] Another function of VGAM958 is therefore inhibition of LOC146243 (Accession XM_096956). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146243. LOC147077 (Accession XM_085699) is another VGAM958 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, designated SEQ ID:38296, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35989] Another function of VGAM958 is therefore inhibition of LOC147077 (Accession XM_085699). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147077. LOC149127 (Accession XM_097584) is another VGAM958 host target gene. LOC149127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149127 BINDING SITE, designated SEQ ID:40952, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35990] Another function of VGAM958 is therefore inhibition of LOC149127 (Accession XM_097584). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149127. LOC149271 (Accession XM_086475) is an-

other VGAM958 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38685, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35991] Another function of VGAM958 is therefore inhibition of LOC149271 (Accession XM_086475). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149271. LOC152343 (Accession XM_087441) is another VGAM958 host target gene. LOC152343 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152343 BINDING SITE, designated SEQ ID:39262, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35992] Another function of VGAM958 is therefore inhibition of LOC152343 (Accession XM_087441). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152343. LOC152905 (Accession XM_017966) is another VGAM958 host target gene. LOC152905 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152905, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152905 BINDING SITE, designated SEQ ID:30332, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35993] Another function of VGAM958 is therefore inhibition of LOC152905 (Accession XM_017966). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152905. LOC153232 (Accession XM_098331) is another VGAM958 host target gene. LOC153232 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153232, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153232 BINDING SITE, designated SEQ ID:41599, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35994] Another function of VGAM958 is therefore inhibition of LOC153232 (Accession XM_098331). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153232. LOC157657 (Accession XM_088352) is another VGAM958 host target gene. LOC157657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157657 BINDING SITE, designated SEQ ID:39628, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35995] Another function of VGAM958 is therefore inhibition of LOC157657 (Accession XM_088352). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157657. LOC157737 (Accession XM_098819) is another VGAM958 host target gene. LOC157737 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157737 BINDING SITE, designated SEQ ID:41844, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35996] Another function of VGAM958 is therefore inhibition of LOC157737 (Accession XM_098819). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157737. LOC158230 (Accession XM_088517) is another VGAM958 host target gene. LOC158230 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158230 BINDING SITE, designated SEQ ID:39768, to the nucleotide sequence of VGAM958 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3669.

[35997] Another function of VGAM958 is therefore inhibition of LOC158230 (Accession XM_088517). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158230. LOC165693 (Accession XM_093373) is another VGAM958 host target gene. LOC165693 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165693 BINDING SITE, designated SEQ ID:40189, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35998] Another function of VGAM958 is therefore inhibition of LOC165693 (Accession XM_093373). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165693. LOC169026 (Accession XM_095471) is another VGAM958 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169026, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40270, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[35999] Another function of VGAM958 is therefore inhibition of LOC169026 (Accession XM_095471). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. LOC196074 (Accession XM_113647) is another VGAM958 host target gene. LOC196074 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196074 BINDING SITE, designated SEQ ID:42323, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36000] Another function of VGAM958 is therefore inhibition of LOC196074 (Accession XM_113647). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC196074. LOC200058 (Accession XM_114109) is another VGAM958 host target gene. LOC200058 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200058 BINDING SITE, designated SEQ ID:42703, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36001] Another function of VGAM958 is therefore inhibition of LOC200058 (Accession XM_114109). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200058. LOC202152 (Accession XM_114446) is another VGAM958 host target gene. LOC202152 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202152 BINDING SITE, designated SEQ ID:42966, to

the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36002] Another function of VGAM958 is therefore inhibition of LOC202152 (Accession XM_114446). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202152. LOC220522 (Accession XM_018306) is another VGAM958 host target gene. LOC220522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220522 BINDING SITE, designated SEQ ID:30355, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36003] Another function of VGAM958 is therefore inhibition of LOC220522 (Accession XM_018306). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220522. LOC220753 (Accession XM_167549) is another VGAM958 host target gene. LOC220753 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220753 BINDING SITE, designated SEQ ID:44664, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36004] Another function of VGAM958 is therefore inhibition of LOC220753 (Accession XM_167549). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220753. LOC253258 (Accession XM_172870) is another VGAM958 host target gene. LOC253258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253258 BINDING SITE, designated SEQ ID:46149, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36005] Another function of VGAM958 is therefore inhibition of LOC253258 (Accession XM_172870). Accordingly, utilities

of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253258. LOC253612 (Accession XM_172985) is another VGAM958 host target gene. LOC253612 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253612 BINDING SITE, designated SEQ ID:46258, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36006] Another function of VGAM958 is therefore inhibition of LOC253612 (Accession XM_172985). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253612. LOC255057 (Accession XM_170903) is another VGAM958 host target gene. LOC255057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC255057 BINDING SITE, designated SEQ ID:45663, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36007] Another function of VGAM958 is therefore inhibition of LOC255057 (Accession XM_170903). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255057. LOC257482 (Accession XM_168544) is another VGAM958 host target gene. LOC257482 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257482 BINDING SITE, designated SEQ ID:45237, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36008] Another function of VGAM958 is therefore inhibition of LOC257482 (Accession XM_168544). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257482. LOC90494 (Accession XM_032161) is another VGAM958 host target gene. LOC90494 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90494 BINDING SITE, designated SEQ ID:31578, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36009] Another function of VGAM958 is therefore inhibition of LOC90494 (Accession XM_032161). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90494. LOC92405 (Accession XM_044914) is another VGAM958 host target gene. LOC92405 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92405 BINDING SITE, designated SEQ ID:34305, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36010] Another function of VGAM958 is therefore inhibition of

LOC92405 (Accession XM_044914). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92405. LOC92578 (Accession XM_045900) is another VGAM958 host target gene. LOC92578 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92578, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92578 BINDING SITE, designated SEQ ID:34608, to the nucleotide sequence of VGAM958 RNA, herein designated VGAM RNA, also designated SEQ ID:3669.

[36011] Another function of VGAM958 is therefore inhibition of LOC92578 (Accession XM_045900). Accordingly, utilities of VGAM958 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92578. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 959 (VGAM959) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[36012] VGAM959 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM959 was detected is described hereinabove with reference to Figs. 1–8.

[36013] VGAM959 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Lumpy Skin Disease Virus. VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36014] VGAM959 gene encodes a VGAM959 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM959 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM959 precursor RNA is designated SEQ ID:945, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:945 is located at position 24838 relative to the genome of Lumpy Skin Disease Virus.

[36015] VGAM959 precursor RNA folds onto itself, forming VGAM959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36016] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM959 folded precursor RNA into VGAM959 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 59%) nucleotide se-
quence of VGAM959 RNA is designated SEQ ID:3670, and
is provided hereinbelow with reference to the sequence
listing part.

[36017] VGAM959 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM959 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM959 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[36018] VGAM959 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM959 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM959 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[36019] The complementary binding of VGAM959 RNA, herein designated VGAM RNA, to host target binding sites on VGAM959 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM959 host target RNA into VGAM959 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36020] It is appreciated that VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM959 host target genes. The mRNA of each one of this plurality of VGAM959 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM959 RNA, herein designated VGAM RNA, and which when bound by VGAM959 RNA causes inhibition of translation of respective one or more VGAM959 host target proteins.

[36021] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM959 gene, herein designated VGAM GENE, on one or

more VGAM959 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36022] It is yet further appreciated that a function of VGAM959 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of viral infection by Lumpy Skin Disease Virus. Specific functions, and accordingly utilities, of VGAM959 correlate with, and may be deduced from, the identity of the host target genes which VGAM959 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [36023] Nucleotide sequences of the VGAM959 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM959 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM959 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM959 are further described hereinbelow with reference to Table 1.
- [36024] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM959 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM959 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36025] As mentioned hereinabove with reference to Fig. 1, a function of VGAM959 gene, herein designated VGAM is inhibition of expression of VGAM959 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM959 correlate with, and may be deduced from, the identity of the target genes which VGAM959 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [36026] High-mobility Group Nucleosome Binding Domain 1

(HMGN1, Accession NM_004965) is a VGAM959 host target gene. HMGN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGN1 BINDING SITE, designated SEQ ID:11411, to the nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, also designated SEQ ID:3670.

[36027] A function of VGAM959 is therefore inhibition of High-mobility Group Nucleosome Binding Domain 1 (HMGN1, Accession NM_004965), a gene which binds to the inner side of the nucleosomal DNA and involves in transcriptional regulation. Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGN1. The function of HMGN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.PIG8 (Accession NM_004879) is another VGAM959 host target gene. PIG8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by PIG8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIG8 BINDING SITE, designated SEQ ID:11314, to the nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, also designated SEQ ID:3670.

[36028] Another function of VGAM959 is therefore inhibition of PIG8 (Accession NM_004879), a gene which is induced by p53 and may be involved in apoptosis. Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIG8. The function of PIG8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM737. KIAA1095 (Accession XM_041363) is another VGAM959 host target gene. KIAA1095 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1095 BINDING SITE, designated SEQ ID:33504, to the

nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, also designated SEQ ID:3670.

[36029] Another function of VGAM959 is therefore inhibition of KIAA1095 (Accession XM_041363). Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1095. LOC145854 (Accession XM_085259) is another VGAM959 host target gene. LOC145854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145854 BINDING SITE, designated SEQ ID:38004, to the nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, also designated SEQ ID:3670.

[36030] Another function of VGAM959 is therefore inhibition of LOC145854 (Accession XM_085259). Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145854. LOC158956 (Accession XM_039450) is another VGAM959 host target gene. LOC158956 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC158956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158956 BINDING SITE, designated SEQ ID:33095, to the nucleotide sequence of VGAM959 RNA, herein designated VGAM RNA, also designated SEQ ID:3670.

[36031] Another function of VGAM959 is therefore inhibition of LOC158956 (Accession XM_039450). Accordingly, utilities of VGAM959 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158956. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 960 (VGAM960) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36032] VGAM960 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM960 was detected is described hereinabove with reference to Figs. 1–8.

[36033] VGAM960 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Lumpy Skin Disease Virus. VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36034] VGAM960 gene encodes a VGAM960 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM960 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM960 precursor RNA is designated SEQ ID:946, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:946 is located at position 28243 relative to the genome of Lumpy Skin Disease Virus.

[36035] VGAM960 precursor RNA folds onto itself, forming VGAM960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36036] An enzyme complex designated DICER COMPLEX, `dices` the VGAM960 folded precursor RNA into VGAM960 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM960 RNA is designated SEQ ID:3671, and is provided hereinbelow with reference to the sequence listing part.

[36037] VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM960 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36038] VGAM960 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM960 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM960 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36039] The complementary binding of VGAM960 RNA, herein designated VGAM RNA, to host target binding sites on VGAM960 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM960 host tar-

get RNA into VGAM960 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36040] It is appreciated that VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM960 host target genes. The mRNA of each one of this plurality of VGAM960 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM960 RNA, herein designated VGAM RNA, and which when bound by VGAM960 RNA causes inhibition of translation of respective one or more VGAM960 host target proteins.

[36041] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM960 gene, herein designated VGAM GENE, on one or more VGAM960 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36042] It is yet further appreciated that a function of VGAM960 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM960 include diagnosis, prevention and treatment of viral infection by Lumpy Skin Disease Virus. Specific functions, and accordingly utilities, of VGAM960 correlate with, and may be deduced from, the identity of the host target genes which VGAM960 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36043] Nucleotide sequences of the VGAM960 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM960 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM960 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM960 are further

described hereinbelow with reference to Table 1.

[36044] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM960 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM960 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36045] As mentioned hereinabove with reference to Fig. 1, a function of VGAM960 gene, herein designated VGAM is inhibition of expression of VGAM960 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM960 correlate with, and may be deduced from, the identity of the target genes which VGAM960 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36046] Asparaginyl-tRNA Synthetase (NARS, Accession NM_004539) is a VGAM960 host target gene. NARS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NARS

BINDING SITE, designated SEQ ID:10890, to the nucleotide sequence of VGAM960 RNA, herein designated VGAM RNA, also designated SEQ ID:3671.

[36047] A function of VGAM960 is therefore inhibition of Asparaginyl-tRNA Synthetase (NARS, Accession NM_004539), a gene which is ASPARAGINYL-tRNA SYNTHETASE. Accordingly, utilities of VGAM960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NARS. The function of NARS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM601. Solute Carrier Family 16 (monocarboxylic acid transporters), Member 2 (putative transporter) (SLC16A2, Accession NM_006517) is another VGAM960 host target gene. SLC16A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC16A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC16A2 BINDING SITE, designated SEQ ID:13272, to the nucleotide sequence of VGAM960 RNA, herein designated VGAM RNA, also designated SEQ

ID:3671.

[36048] Another function of VGAM960 is therefore inhibition of Solute Carrier Family 16 (monocarboxylic acid transporters), Member 2 (putative transporter) (SLC16A2, Accession NM_006517). Accordingly, utilities of VGAM960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC16A2.

KIAA0391 (Accession NM_014672) is another VGAM960 host target gene. KIAA0391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0391 BINDING SITE, designated SEQ ID:16137, to the nucleotide sequence of VGAM960 RNA, herein designated VGAM RNA, also designated SEQ ID:3671.

[36049] Another function of VGAM960 is therefore inhibition of KIAA0391 (Accession NM_014672). Accordingly, utilities of VGAM960 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0391. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 961 (VGAM961) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36050] VGAM961 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM961 was detected is described hereinabove with reference to Figs. 1–8.

[36051] VGAM961 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Goatpox Virus. VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36052] VGAM961 gene encodes a VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM961 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM961 precursor RNA is designated SEQ ID:947, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:947 is located at position 23299 relative to the genome of Goat–

pox Virus.

[36053] VGAM961 precursor RNA folds onto itself, forming VGAM961 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36054] An enzyme complex designated DICER COMPLEX, `dices` the VGAM961 folded precursor RNA into VGAM961 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM961 RNA is designated SEQ ID:3672, and is provided hereinbelow with reference to the sequence listing part.

[36055] VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM961 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36056] VGAM961 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM961 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM961 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36057] The complementary binding of VGAM961 RNA, herein designated VGAM RNA, to host target binding sites on VGAM961 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM961 host target RNA into VGAM961 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36058] It is appreciated that VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM961 host target genes. The mRNA of each one of this plurality of VGAM961 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM961 RNA, herein designated VGAM RNA, and which when bound by VGAM961 RNA causes inhibition of translation of respective one or more VGAM961 host target proteins.

[36059] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM961 gene, herein designated VGAM GENE, on one or more VGAM961 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36060] It is yet further appreciated that a function of VGAM961 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM961 include diagnosis, prevention and treatment of viral infection by Goatpox Virus. Specific functions, and accordingly utilities, of VGAM961 correlate

with, and may be deduced from, the identity of the host target genes which VGAM961 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36061] Nucleotide sequences of the VGAM961 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM961 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM961 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM961 are further described hereinbelow with reference to Table 1.

[36062] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM961 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM961 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36063] As mentioned hereinabove with reference to Fig. 1, a function of VGAM961 gene, herein designated VGAM is inhibition of expression of VGAM961 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM961 correlate with, and may be deduced

from, the identity of the target genes which VGAM961 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36064] Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858) is a VGAM961 host target gene. COL19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL19A1 BINDING SITE, designated SEQ ID:7596, to the nucleotide sequence of VGAM961 RNA, herein designated VGAM RNA, also designated SEQ ID:3672.

[36065] A function of VGAM961 is therefore inhibition of Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858), a gene which may act as a cross-bridge between fibrils and other extracellular matrix molecules. Accordingly, utilities of VGAM961 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL19A1. The function of COL19A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM19. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 962 (VGAM962) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36066] VGAM962 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM962 was detected is described hereinabove with reference to Figs. 1–8.

[36067] VGAM962 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36068] VGAM962 gene encodes a VGAM962 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM962 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM962 precursor RNA is designated SEQ ID:948, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:948 is located at position 22678 relative to the genome of Meleagrid Herpesvirus 1.

[36069] VGAM962 precursor RNA folds onto itself, forming VGAM962 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36070] An enzyme complex designated DICER COMPLEX, `dices` the VGAM962 folded precursor RNA into VGAM962 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM962 RNA is designated SEQ ID:3673, and is provided hereinbelow with reference to the sequence listing part.

[36071] VGAM962 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM962 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36072] VGAM962 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM962 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM962 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36073] The complementary binding of VGAM962 RNA, herein designated VGAM RNA, to host target binding sites on VGAM962 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM962 host target RNA into VGAM962 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36074] It is appreciated that VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM962 host target genes. The mRNA of each one of this plurality of VGAM962 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM962 RNA, herein designated VGAM RNA, and which when bound by VGAM962 RNA causes in-

hibition of translation of respective one or more VGAM962 host target proteins.

[36075] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM962 gene, herein designated VGAM GENE, on one or more VGAM962 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36076] It is yet further appreciated that a function of VGAM962 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM962 include diagnosis, prevention and

treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM962 correlate with, and may be deduced from, the identity of the host target genes which VGAM962 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36077] Nucleotide sequences of the VGAM962 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM962 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM962 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM962 are further described hereinbelow with reference to Table 1.

[36078] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM962 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM962 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36079] As mentioned hereinabove with reference to Fig. 1, a function of VGAM962 gene, herein designated VGAM is inhibition of expression of VGAM962 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM962 correlate with, and may be deduced from, the identity of the target genes which VGAM962 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36080] Adenylate Cyclase 7 (ADCY7, Accession NM_001114) is a VGAM962 host target gene. ADCY7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY7 BINDING SITE, designated SEQ ID:6778, to the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, also designated SEQ ID:3673.

[36081] A function of VGAM962 is therefore inhibition of Adenylate Cyclase 7 (ADCY7, Accession NM_001114), a gene which this is a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY7. The function of ADCY7 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM108. Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444) is another VGAM962 host target gene. CHRAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRAC1 BINDING SITE, designated SEQ ID:18901, to the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, also designated SEQ ID:3673.

[36082] Another function of VGAM962 is therefore inhibition of Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444). Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRAC1. KIAA1538 (Accession XM_049474) is another VGAM962 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35421, to the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, also designated SEQ ID:3673.

[36083] Another function of VGAM962 is therefore inhibition of KIAA1538 (Accession XM_049474). Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. MGC2752 (Accession XM_085842) is another VGAM962 host target gene. MGC2752 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2752, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2752 BINDING SITE, designated SEQ ID:38366, to the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, also designated SEQ ID:3673.

[36084] Another function of VGAM962 is therefore inhibition of MGC2752 (Accession XM_085842). Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2752. LOC146445 (Accession XM_096999) is another

VGAM962 host target gene. LOC146445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146445 BINDING SITE, designated SEQ ID:40697, to the nucleotide sequence of VGAM962 RNA, herein designated VGAM RNA, also designated SEQ ID:3673.

[36085] Another function of VGAM962 is therefore inhibition of LOC146445 (Accession XM_096999). Accordingly, utilities of VGAM962 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146445. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 963 (VGAM963) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36086] VGAM963 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM963 was detected is described

hereinabove with reference to Figs. 1–8.

[36087] VGAM963 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36088] VGAM963 gene encodes a VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM963 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM963 precursor RNA is designated SEQ ID:949, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:949 is located at position 20617 relative to the genome of Meleagrid Herpesvirus 1.

[36089] VGAM963 precursor RNA folds onto itself, forming VGAM963 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36090] An enzyme complex designated DICER COMPLEX, `dices` the VGAM963 folded precursor RNA into VGAM963 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM963 RNA is designated SEQ ID:3674, and is provided hereinbelow with reference to the sequence listing part.

[36091] VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM963 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36092] VGAM963 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM963 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM963 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM963 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36093] The complementary binding of VGAM963 RNA, herein designated VGAM RNA, to host target binding sites on VGAM963 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM963 host target RNA into VGAM963 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36094] It is appreciated that VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM963 host target genes. The mRNA of each one of this plurality of VGAM963 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM963 RNA, herein designated VGAM RNA, and which when bound by VGAM963 RNA causes inhibition of translation of respective one or more VGAM963 host target proteins.

[36095] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM963 gene, herein designated VGAM GENE, on one or more VGAM963 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36096] It is yet further appreciated that a function of VGAM963 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM963 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM963 correlate with, and may be deduced from, the identity of the host target genes which VGAM963 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36097] Nucleotide sequences of the VGAM963 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM963 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM963 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM963 are further described hereinbelow with reference to Table 1.

[36098] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM963 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM963 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36099] As mentioned hereinabove with reference to Fig. 1, a function of VGAM963 gene, herein designated VGAM is inhibition of expression of VGAM963 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM963 correlate with, and may be deduced from, the identity of the target genes which VGAM963 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36100] EZFIT (Accession NM_021216) is a VGAM963 host target gene. EZFIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZFIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of EZFIT BINDING SITE, designated SEQ ID:22197, to the nucleotide sequence of VGAM963 RNA, herein designated VGAM RNA, also designated SEQ ID:3674.

[36101] A function of VGAM963 is therefore inhibition of EZFIT (Accession NM_021216). Accordingly, utilities of VGAM963 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZFIT. KIAA0009 (Accession NM_014637) is another VGAM963 host target gene. KIAA0009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0009 BINDING SITE, designated SEQ ID:16024, to the nucleotide sequence of VGAM963 RNA, herein designated VGAM RNA, also designated SEQ ID:3674.

[36102] Another function of VGAM963 is therefore inhibition of KIAA0009 (Accession NM_014637). Accordingly, utilities of VGAM963 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0009. Ubinuclein 1 (UBN1, Accession NM_016936) is

another VGAM963 host target gene. UBN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBN1 BINDING SITE, designated SEQ ID:18853, to the nucleotide sequence of VGAM963 RNA, herein designated VGAM RNA, also designated SEQ ID:3674.

[36103] Another function of VGAM963 is therefore inhibition of Ubinuclein 1 (UBN1, Accession NM_016936). Accordingly, utilities of VGAM963 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBN1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 964 (VGAM964) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36104] VGAM964 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM964 was detected is described

hereinabove with reference to Figs. 1–8.

[36105] VGAM964 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36106] VGAM964 gene encodes a VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM964 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM964 precursor RNA is designated SEQ ID:950, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:950 is located at position 22865 relative to the genome of Meleagrid Herpesvirus 1.

[36107] VGAM964 precursor RNA folds onto itself, forming VGAM964 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36108] An enzyme complex designated DICER COMPLEX, `dices` the VGAM964 folded precursor RNA into VGAM964 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM964 RNA is designated SEQ ID:3675, and is provided hereinbelow with reference to the sequence listing part.

[36109] VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM964 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36110] VGAM964 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM964 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM964 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM964 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36111] The complementary binding of VGAM964 RNA, herein designated VGAM RNA, to host target binding sites on VGAM964 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM964 host target RNA into VGAM964 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36112] It is appreciated that VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM964 host target genes. The mRNA of each one of this plurality of VGAM964 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM964 RNA, herein designated VGAM RNA, and which when bound by VGAM964 RNA causes inhibition of translation of respective one or more VGAM964 host target proteins.

[36113] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM964 gene, herein designated VGAM GENE, on one or more VGAM964 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36114] It is yet further appreciated that a function of VGAM964 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM964 correlate with, and may be deduced from, the identity of the host target genes which VGAM964 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36115] Nucleotide sequences of the VGAM964 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM964 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM964 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM964 are further described hereinbelow with reference to Table 1.

[36116] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM964 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM964 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36117] As mentioned hereinabove with reference to Fig. 1, a function of VGAM964 gene, herein designated VGAM is inhibition of expression of VGAM964 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM964 correlate with, and may be deduced from, the identity of the target genes which VGAM964 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36118] Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM_007332) is a VGAM964 host target gene. ANKTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKTM1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKTM1 BINDING SITE, designated SEQ ID:14257, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36119] A function of VGAM964 is therefore inhibition of Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM_007332), a gene which attaches integral membrane proteins to cytoskeletal elements. Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKTM1. The function of ANKTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644. Checkpoint Suppressor 1 (CHES1, Accession NM_005197) is another VGAM964 host target gene. CHES1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHES1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHES1 BINDING SITE, designated SEQ

ID:11696, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36120] Another function of VGAM964 is therefore inhibition of Checkpoint Suppressor 1 (CHES1, Accession NM_005197). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHES1. Deoxyguanosine Kinase (DGUOK, Accession NM_080915) is another VGAM964 host target gene. DGUOK BINDING SITE1 and DGUOK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DGUOK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGUOK BINDING SITE1 and DGUOK BINDING SITE2, designated SEQ ID:28136 and SEQ ID:28139 respectively, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36121] Another function of VGAM964 is therefore inhibition of Deoxyguanosine Kinase (DGUOK, Accession NM_080915), a gene which is deoxyguanosine kinase and mediates phosphorylation of several deoxyribonucleosides. Accord-

ingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGUOK. The function of DGUOK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM121. Zinc Finger Protein 202 (ZNF202, Accession NM_003455) is another VGAM964 host target gene. ZNF202 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF202, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF202 BINDING SITE, designated SEQ ID:9508, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36122] Another function of VGAM964 is therefore inhibition of Zinc Finger Protein 202 (ZNF202, Accession NM_003455). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF202. Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM_024331) is another VGAM964 host target gene. C20orf121 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING SITE, designated SEQ ID:23632, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36123] Another function of VGAM964 is therefore inhibition of Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM_024331). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121.

FLJ14213 (Accession NM_024841) is another VGAM964 host target gene. FLJ14213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14213 BINDING SITE, designated SEQ ID:24254, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36124] Another function of VGAM964 is therefore inhibition of FLJ14213 (Accession NM_024841). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14213. FLJ22794 (Accession XM_166220) is another VGAM964 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44030, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36125] Another function of VGAM964 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_006625) is another VGAM964 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:13409, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36126] Another function of VGAM964 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_006625). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. HCA4 (Accession XM_085287) is another VGAM964 host target gene. HCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38018, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36127] Another function of VGAM964 is therefore inhibition of HCA4 (Accession XM_085287). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with HCA4.

KIAA0157 (Accession NM_032182) is another VGAM964 host target gene. KIAA0157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0157 BINDING SITE, designated SEQ ID:25899, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36128] Another function of VGAM964 is therefore inhibition of KIAA0157 (Accession NM_032182). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0157. KIAA0310 (Accession XM_088459) is another VGAM964 host target gene. KIAA0310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0310 BINDING SITE, designated SEQ ID:39710, to the

nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36129] Another function of VGAM964 is therefore inhibition of KIAA0310 (Accession XM_088459). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0310. KIAA0884 (Accession XM_046660) is another VGAM964 host target gene. KIAA0884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0884 BINDING SITE, designated SEQ ID:34772, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36130] Another function of VGAM964 is therefore inhibition of KIAA0884 (Accession XM_046660). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0884. KIAA1077 (Accession XM_053496) is another VGAM964 host target gene. KIAA1077 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA1077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1077 BINDING SITE, designated SEQ ID:36095, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36131] Another function of VGAM964 is therefore inhibition of KIAA1077 (Accession XM_053496). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1077. KIAA1948 (Accession XM_091984) is another VGAM964 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40076, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36132] Another function of VGAM964 is therefore inhibition of KIAA1948 (Accession XM_091984). Accordingly, utilities

of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. LOC151556 (Accession XM_087239) is another VGAM964 host target gene. LOC151556 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151556 BINDING SITE, designated SEQ ID:39133, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36133] Another function of VGAM964 is therefore inhibition of LOC151556 (Accession XM_087239). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151556. LOC256946 (Accession XM_170543) is another VGAM964 host target gene. LOC256946 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC256946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256946 BINDING SITE, designated SEQ ID:45359, to the nucleotide sequence of VGAM964 RNA, herein designated VGAM RNA, also designated SEQ ID:3675.

[36134] Another function of VGAM964 is therefore inhibition of LOC256946 (Accession XM_170543). Accordingly, utilities of VGAM964 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256946. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 965 (VGAM965) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36135] VGAM965 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM965 was detected is described hereinabove with reference to Figs. 1–8.

[36136] VGAM965 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36137] VGAM965 gene encodes a VGAM965 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM965 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM965 precursor RNA is designated SEQ ID:951, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:951 is located at position 23173 relative to the genome of Meleagrid Herpesvirus 1.

[36138] VGAM965 precursor RNA folds onto itself, forming VGAM965 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36139] An enzyme complex designated DICER COMPLEX, `dices` the VGAM965 folded precursor RNA into VGAM965 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM965 RNA is designated SEQ ID:3676, and is provided hereinbelow with reference to the sequence listing part.

[36140] VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM965 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36141] VGAM965 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM965 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM965 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[36142] The complementary binding of VGAM965 RNA, herein designated VGAM RNA, to host target binding sites on VGAM965 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM965 host target RNA into VGAM965 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36143] It is appreciated that VGAM965 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM965 host target genes. The mRNA of each one of this plurality of VGAM965 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM965 RNA, herein designated VGAM RNA, and which when bound by VGAM965 RNA causes inhibition of translation of respective one or more VGAM965 host target proteins.

[36144] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM965 gene, herein designated VGAM GENE, on one or more VGAM965 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[36145] It is yet further appreciated that a function of VGAM965 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM965 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM965 correlate with, and may be deduced from, the identity of the host target genes which VGAM965 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36146] Nucleotide sequences of the VGAM965 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM965 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM965 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM965 are further described hereinbelow with reference to Table 1.

[36147] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM965 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM965 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36148] As mentioned hereinabove with reference to Fig. 1, a function of VGAM965 gene, herein designated VGAM is inhibition of expression of VGAM965 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM965 correlate with, and may be deduced from, the identity of the target genes which VGAM965 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36149] Holocarboxylase Synthetase
(biotin-[propionyl-Coenzyme A-carboxylase
(ATP-hydrolysing)] Ligase) (HLCS, Accession NM_000411)
is a VGAM965 host target gene. HLCS BINDING SITE is
HOST TARGET binding site found in the 3' untranslated
region of mRNA encoded by HLCS, corresponding to a
HOST TARGET binding site such as BINDING SITE I, BIND-
ING SITE II or BINDING SITE III. Table 2 illustrates the com-
plementarity of the nucleotide sequences of HLCS BIND-
ING SITE, designated SEQ ID:5990, to the nucleotide se-
quence of VGAM965 RNA, herein designated VGAM RNA,

also designated SEQ ID:3676.

[36150] A function of VGAM965 is therefore inhibition of Holocarboxylase Synthetase (biotin-[propionyl-Coenzyme A-carboxylase (ATP-hydrolysing)] Ligase) (HLCS, Accession NM_000411). Accordingly, utilities of VGAM965 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLCS. Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456) is another VGAM965 host target gene. C13orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C13orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C13orf1 BINDING SITE, designated SEQ ID:21688, to the nucleotide sequence of VGAM965 RNA, herein designated VGAM RNA, also designated SEQ ID:3676.

[36151] Another function of VGAM965 is therefore inhibition of Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456). Accordingly, utilities of VGAM965 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C13orf1. DK-FZp761B1514 (Accession NM_032288) is another

VGAM965 host target gene. DKFZp761B1514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B1514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B1514 BINDING SITE, designated SEQ ID:26045, to the nucleotide sequence of VGAM965 RNA, herein designated VGAM RNA, also designated SEQ ID:3676.

[36152] Another function of VGAM965 is therefore inhibition of DKFZp761B1514 (Accession NM_032288). Accordingly, utilities of VGAM965 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B1514. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 966 (VGAM966) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36153] VGAM966 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM966 was detected is described hereinabove with reference to Figs. 1–8.

[36154] VGAM966 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36155] VGAM966 gene encodes a VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM966 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM966 precursor RNA is designated SEQ ID:952, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:952 is located at position 21558 relative to the genome of Meleagrid Herpesvirus 1.

[36156] VGAM966 precursor RNA folds onto itself, forming VGAM966 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36157] An enzyme complex designated DICER COMPLEX, `dices` the VGAM966 folded precursor RNA into VGAM966 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM966 RNA is designated SEQ ID:3677, and is provided hereinbelow with reference to the sequence listing part.

[36158] VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM966 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36159] VGAM966 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM966 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM966 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[36160] The complementary binding of VGAM966 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM966 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM966 host target RNA into VGAM966 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36161] It is appreciated that VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM966 host target genes. The mRNA of each one of this plurality of VGAM966 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM966 RNA, herein designated VGAM RNA, and which when bound by VGAM966 RNA causes inhibition of translation of respective one or more VGAM966 host target proteins.

[36162] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM966 gene, herein designated VGAM GENE, on one or more VGAM966 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36163] It is yet further appreciated that a function of VGAM966 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM966 correlate with, and may be deduced from, the identity of the host target genes which VGAM966 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36164] Nucleotide sequences of the VGAM966 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM966 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM966 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM966 are further described hereinbelow with reference to Table 1.

[36165] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM966 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM966 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36166] As mentioned hereinabove with reference to Fig. 1, a function of VGAM966 gene, herein designated VGAM is inhibition of expression of VGAM966 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM966 correlate with, and may be deduced from, the identity of the target genes which VGAM966 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36167] Erythrocyte Membrane Protein Band 4.1-like 2 (EPB41L2, Accession NM_001431) is a VGAM966 host target gene. EPB41L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

EPB41L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L2 BINDING SITE, designated SEQ ID:7154, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36168] A function of VGAM966 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 2 (EPB41L2, Accession NM_001431). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L2. Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM_000322) is another VGAM966 host target gene. RDS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDS BINDING SITE, designated SEQ ID:5863, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36169] Another function of VGAM966 is therefore inhibition of

Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM_000322), a gene which may function as an adhesion molecule involved in stabilization and compaction of outer segment disks or in the maintenance of the curvature of the rim. Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDS. The function of RDS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341.KIAA1946 (Accession XM_092459) is another VGAM966 host target gene. KIAA1946 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1946 BINDING SITE, designated SEQ ID:40118, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36170] Another function of VGAM966 is therefore inhibition of KIAA1946 (Accession XM_092459). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1946. MGC3130 (Accession NM_024032) is another VGAM966 host target gene. MGC3130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3130 BINDING SITE, designated SEQ ID:23460, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36171] Another function of VGAM966 is therefore inhibition of MGC3130 (Accession NM_024032). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3130. MGC4415 (Accession NM_031484) is another VGAM966 host target gene. MGC4415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4415 BINDING SITE, designated SEQ ID:25566, to the nucleotide

sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36172] Another function of VGAM966 is therefore inhibition of MGC4415 (Accession NM_031484). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4415. PRO0611 (Accession NM_014076) is another VGAM966 host target gene. PRO0611 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0611, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0611 BINDING SITE, designated SEQ ID:15304, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36173] Another function of VGAM966 is therefore inhibition of PRO0611 (Accession NM_014076). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0611. LOC63929 (Accession NM_022098) is another VGAM966 host target gene. LOC63929 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by LOC63929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC63929 BINDING SITE, designated SEQ ID:22639, to the nucleotide sequence of VGAM966 RNA, herein designated VGAM RNA, also designated SEQ ID:3677.

[36174] Another function of VGAM966 is therefore inhibition of LOC63929 (Accession NM_022098). Accordingly, utilities of VGAM966 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC63929. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 967 (VGAM967) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36175] VGAM967 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM967 was detected is described hereinabove with reference to Figs. 1–8.

[36176] VGAM967 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Sheeppox Virus.

VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36177] VGAM967 gene encodes a VGAM967 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM967 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM967 precursor RNA is designated SEQ ID:953, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:953 is located at position 26912 relative to the genome of Sheeppox Virus.

[36178] VGAM967 precursor RNA folds onto itself, forming VGAM967 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36179] An enzyme complex designated DICER COMPLEX, `dices` the VGAM967 folded precursor RNA into VGAM967 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM967 RNA is designated SEQ ID:3678, and is provided hereinbelow with reference to the sequence listing part.

[36180] VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM967 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36181] VGAM967 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM967 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM967 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36182] The complementary binding of VGAM967 RNA, herein designated VGAM RNA, to host target binding sites on VGAM967 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM967 host tar-

get RNA into VGAM967 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36183] It is appreciated that VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM967 host target genes. The mRNA of each one of this plurality of VGAM967 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM967 RNA, herein designated VGAM RNA, and which when bound by VGAM967 RNA causes inhibition of translation of respective one or more VGAM967 host target proteins.

[36184] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM967 gene, herein designated VGAM GENE, on one or more VGAM967 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36185] It is yet further appreciated that a function of VGAM967 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGAM967 correlate with, and may be deduced from, the identity of the host target genes which VGAM967 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36186] Nucleotide sequences of the VGAM967 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM967 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM967 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM967 are further

described hereinbelow with reference to Table 1.

[36187] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM967 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM967 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36188] As mentioned hereinabove with reference to Fig. 1, a function of VGAM967 gene, herein designated VGAM is inhibition of expression of VGAM967 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM967 correlate with, and may be deduced from, the identity of the target genes which VGAM967 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36189] LOC161589 (Accession XM_090991) is a VGAM967 host target gene. LOC161589 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161589 BINDING SITE,

designated SEQ ID:40023, to the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, also designated SEQ ID:3678.

[36190] A function of VGAM967 is therefore inhibition of LOC161589 (Accession XM_090991). Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161589. LOC202108 (Accession XM_114442) is another VGAM967 host target gene. LOC202108 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202108 BINDING SITE, designated SEQ ID:42965, to the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, also designated SEQ ID:3678.

[36191] Another function of VGAM967 is therefore inhibition of LOC202108 (Accession XM_114442). Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202108. LOC202333 (Accession XM_114467) is another VGAM967 host target gene. LOC202333 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202333 BINDING SITE, designated SEQ ID:42970, to the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, also designated SEQ ID:3678.

[36192] Another function of VGAM967 is therefore inhibition of LOC202333 (Accession XM_114467). Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202333. LOC221838 (Accession XM_166521) is another VGAM967 host target gene. LOC221838 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221838 BINDING SITE, designated SEQ ID:44459, to the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, also designated SEQ ID:3678.

[36193] Another function of VGAM967 is therefore inhibition of

LOC221838 (Accession XM_166521). Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221838. LOC221839 (Accession XM_166506) is another VGAM967 host target gene. LOC221839 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221839 BINDING SITE, designated SEQ ID:44430, to the nucleotide sequence of VGAM967 RNA, herein designated VGAM RNA, also designated SEQ ID:3678.

[36194] Another function of VGAM967 is therefore inhibition of LOC221839 (Accession XM_166506). Accordingly, utilities of VGAM967 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221839. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 968 (VGAM968) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[36195] VGAM968 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM968 was detected is described hereinabove with reference to Figs. 1–8.

[36196] VGAM968 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox Virus. VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36197] VGAM968 gene encodes a VGAM968 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM968 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM968 precursor RNA is designated SEQ ID:954, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:954 is located at position 24977 relative to the genome of Sheeppox Virus.

[36198] VGAM968 precursor RNA folds onto itself, forming VGAM968 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36199] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM968 folded precursor RNA into VGAM968 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 42%) nucleotide se-
quence of VGAM968 RNA is designated SEQ ID:3679, and
is provided hereinbelow with reference to the sequence
listing part.

[36200] VGAM968 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM968 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM968 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[36201] VGAM968 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM968 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM968 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[36202] The complementary binding of VGAM968 RNA, herein designated VGAM RNA, to host target binding sites on VGAM968 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM968 host target RNA into VGAM968 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36203] It is appreciated that VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM968 host target genes. The mRNA of each one of this plurality of VGAM968 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM968 RNA, herein designated VGAM RNA, and which when bound by VGAM968 RNA causes inhibition of translation of respective one or more VGAM968 host target proteins.

[36204] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM968 gene, herein designated VGAM GENE, on one or

more VGAM968 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36205] It is yet further appreciated that a function of VGAM968 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGAM968 correlate with, and may be deduced from, the identity of the host target genes which VGAM968 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [36206] Nucleotide sequences of the VGAM968 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM968 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM968 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM968 are further described hereinbelow with reference to Table 1.
- [36207] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM968 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM968 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36208] As mentioned hereinabove with reference to Fig. 1, a function of VGAM968 gene, herein designated VGAM is inhibition of expression of VGAM968 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM968 correlate with, and may be deduced from, the identity of the target genes which VGAM968 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [36209] Mastermind-like 1 (Drosophila) (MAML1, Accession

NM_014757) is a VGAM968 host target gene. MAML1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAML1 BINDING SITE, designated SEQ ID:16496, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, also designated SEQ ID:3679.

[36210] A function of VGAM968 is therefore inhibition of Mastermind-like 1 (Drosophila) (MAML1, Accession NM_014757), a gene which MAML1 functions as a transcriptional coactivator for Notch signaling. Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAML1. The function of MAML1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM556.KIAA0628 (Accession NM_014789) is another VGAM968 host target gene. KIAA0628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0628, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0628 BINDING SITE, designated SEQ ID:16673, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, also designated SEQ ID:3679.

[36211] Another function of VGAM968 is therefore inhibition of KIAA0628 (Accession NM_014789). Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0628. KIAA1281 (Accession XM_114432) is another VGAM968 host target gene. KIAA1281 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1281 BINDING SITE, designated SEQ ID:42963, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, also designated SEQ ID:3679.

[36212] Another function of VGAM968 is therefore inhibition of KIAA1281 (Accession XM_114432). Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1281. MIG (Accession NM_002416) is another VGAM968 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, designated SEQ ID:8245, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, also designated SEQ ID:3679.

[36213] Another function of VGAM968 is therefore inhibition of MIG (Accession NM_002416). Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. LOC222865 (Accession XM_167242) is another VGAM968 host target gene. LOC222865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222865 BINDING SITE, designated SEQ ID:44623, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA,

also designated SEQ ID:3679.

[36214] Another function of VGAM968 is therefore inhibition of LOC222865 (Accession XM_167242). Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222865. LOC92303 (Accession XM_044108) is another VGAM968 host target gene. LOC92303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92303 BINDING SITE, designated SEQ ID:34134, to the nucleotide sequence of VGAM968 RNA, herein designated VGAM RNA, also designated SEQ ID:3679.

[36215] Another function of VGAM968 is therefore inhibition of LOC92303 (Accession XM_044108). Accordingly, utilities of VGAM968 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92303. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 969 (VGAM969) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36216] VGAM969 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM969 was detected is described hereinabove with reference to Figs. 1–8.

[36217] VGAM969 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Goatpox Virus.

VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36218] VGAM969 gene encodes a VGAM969 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM969 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM969 precursor RNA is designated SEQ ID:955, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:955 is located at position 25550 relative to the genome of Goatpox Virus.

[36219] VGAM969 precursor RNA folds onto itself, forming

VGAM969 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36220] An enzyme complex designated DICER COMPLEX, `dices` the VGAM969 folded precursor RNA into VGAM969 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM969 RNA is designated SEQ ID:3680, and is provided hereinbelow with reference to the sequence listing part.

[36221] VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM969 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36222] VGAM969 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM969 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM969 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36223] The complementary binding of VGAM969 RNA, herein designated VGAM RNA, to host target binding sites on VGAM969 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM969 host target RNA into VGAM969 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36224] It is appreciated that VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM969 host target genes. The mRNA of each one of this plurality of VGAM969 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM969 RNA, herein designated VGAM RNA, and which when bound by VGAM969 RNA causes inhibition of translation of respective one or more VGAM969 host target proteins.

[36225] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM969 gene, herein designated VGAM GENE, on one or more VGAM969 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36226] It is yet further appreciated that a function of VGAM969 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM969 include diagnosis, prevention and treatment of viral infection by Goatpox Virus. Specific functions, and accordingly utilities, of VGAM969 correlate with, and may be deduced from, the identity of the host target genes which VGAM969 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[36227] Nucleotide sequences of the VGAM969 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM969 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM969 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM969 are further described hereinbelow with reference to Table 1.

[36228] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM969 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM969 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36229] As mentioned hereinabove with reference to Fig. 1, a function of VGAM969 gene, herein designated VGAM is inhibition of expression of VGAM969 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM969 correlate with, and may be deduced from, the identity of the target genes which VGAM969 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[36230] KIAA0534 (Accession XM_049349) is a VGAM969 host target gene. KIAA0534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0534 BINDING SITE, designated SEQ ID:35375, to the nucleotide sequence of VGAM969 RNA, herein designated VGAM RNA, also designated SEQ ID:3680.

[36231] A function of VGAM969 is therefore inhibition of KIAA0534 (Accession XM_049349). Accordingly, utilities of VGAM969 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0534. KIAA1708 (Accession XM_040211) is another VGAM969 host target gene. KIAA1708 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1708, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1708 BINDING SITE, designated SEQ ID:33271, to the

nucleotide sequence of VGAM969 RNA, herein designated VGAM RNA, also designated SEQ ID:3680.

[36232] Another function of VGAM969 is therefore inhibition of KIAA1708 (Accession XM_040211). Accordingly, utilities of VGAM969 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1708. LOC157464 (Accession XM_098758) is another VGAM969 host target gene. LOC157464 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157464 BINDING SITE, designated SEQ ID:41796, to the nucleotide sequence of VGAM969 RNA, herein designated VGAM RNA, also designated SEQ ID:3680.

[36233] Another function of VGAM969 is therefore inhibition of LOC157464 (Accession XM_098758). Accordingly, utilities of VGAM969 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 970 (VGAM970) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36234] VGAM970 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM970 was detected is described hereinabove with reference to Figs. 1–8.

[36235] VGAM970 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox Virus. VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36236] VGAM970 gene encodes a VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM970 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM970 precursor RNA is designated SEQ ID:956, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:956 is located at position 23426 relative to the genome of Sheeppox Virus.

[36237] VGAM970 precursor RNA folds onto itself, forming VGAM970 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36238] An enzyme complex designated DICER COMPLEX, `dices` the VGAM970 folded precursor RNA into VGAM970 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM970 RNA is designated SEQ ID:3681, and is provided hereinbelow with reference to the sequence listing part.

[36239] VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM970 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM970 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36240] VGAM970 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM970 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM970 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36241] The complementary binding of VGAM970 RNA, herein designated VGAM RNA, to host target binding sites on VGAM970 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM970 host target RNA into VGAM970 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36242] It is appreciated that VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM970 host target genes. The mRNA of each one of this plurality of VGAM970 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM970 RNA, herein designated VGAM RNA, and which when bound by VGAM970 RNA causes inhibition of translation of respective one or more VGAM970 host target proteins.

[36243] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM970 gene, herein designated VGAM GENE, on one or more VGAM970 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36244] It is yet further appreciated that a function of VGAM970 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGAM970 correlate with, and may be deduced from, the identity of the host

target genes which VGAM970 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36245] Nucleotide sequences of the VGAM970 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM970 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM970 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM970 are further described hereinbelow with reference to Table 1.

[36246] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM970 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM970 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36247] As mentioned hereinabove with reference to Fig. 1, a function of VGAM970 gene, herein designated VGAM is inhibition of expression of VGAM970 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM970 correlate with, and may be deduced from, the identity of the target genes which VGAM970

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36248] B29 (Accession NM_031939) is a VGAM970 host target gene. B29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B29 BINDING SITE, designated SEQ ID:25684, to the nucleotide sequence of VGAM970 RNA, herein designated VGAM RNA, also designated SEQ ID:3681.

[36249] A function of VGAM970 is therefore inhibition of B29 (Accession NM_031939). Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B29. CD2-associated Protein (CD2AP, Accession NM_012120) is another VGAM970 host target gene. CD2AP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD2AP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD2AP BINDING SITE, designated SEQ ID:14431, to the nucleotide se-

quence of VGAM970 RNA, herein designated VGAM RNA, also designated SEQ ID:3681.

[36250] Another function of VGAM970 is therefore inhibition of CD2-associated Protein (CD2AP, Accession NM_012120), a gene which binds CAS ligand and may therefor involves in its growth regulatory pathway. Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD2AP. The function of CD2AP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95.Mdm4, Transformed 3T3 Cell Double Minute 4, P53 Binding Protein (mouse) (MDM4, Accession NM_002393) is another VGAM970 host target gene. MDM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDM4 BINDING SITE, designated SEQ ID:8208, to the nucleotide sequence of VGAM970 RNA, herein designated VGAM RNA, also designated SEQ ID:3681.

[36251] Another function of VGAM970 is therefore inhibition of

Mdm4, Transformed 3T3 Cell Double Minute 4, P53 Binding Protein (mouse) (MDM4, Accession NM_002393), a gene which is strongly similar to murine Mdm4; may interact with p53. Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDM4. The function of MDM4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM739. SERP1 (Accession NM_014445) is another VGAM970 host target gene. SERP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERP1 BINDING SITE, designated SEQ ID:15795, to the nucleotide sequence of VGAM970 RNA, herein designated VGAM RNA, also designated SEQ ID:3681.

[36252] Another function of VGAM970 is therefore inhibition of SERP1 (Accession NM_014445). Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERP1.

SKI-like (SKIL, Accession NM_005414) is another VGAM970 host target gene. SKIL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SKIL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIL BINDING SITE, designated SEQ ID:11885, to the nucleotide sequence of VGAM970 RNA, herein designated VGAM RNA, also designated SEQ ID:3681.

[36253] Another function of VGAM970 is therefore inhibition of SKI-like (SKIL, Accession NM_005414). Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIL. LOC149271 (Accession XM_086475) is another VGAM970 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38676, to the nucleotide sequence of VGAM970 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3681.

[36254] Another function of VGAM970 is therefore inhibition of LOC149271 (Accession XM_086475). Accordingly, utilities of VGAM970 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149271. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 971 (VGAM971) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36255] VGAM971 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM971 was detected is described hereinabove with reference to Figs. 1–8.

[36256] VGAM971 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36257] VGAM971 gene encodes a VGAM971 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM971 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM971 precursor RNA is designated SEQ ID:957, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:957 is located at position 53540 relative to the genome of *Melanoplus Sanguinipes* Entomopoxvirus.

[36258] VGAM971 precursor RNA folds onto itself, forming VGAM971 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36259] An enzyme complex designated DICER COMPLEX, `dices` the VGAM971 folded precursor RNA into VGAM971 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM971 RNA is designated SEQ ID:3682, and is provided hereinbelow with reference to the sequence listing part.

[36260] VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM971 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36261] VGAM971 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM971 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM971 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36262] The complementary binding of VGAM971 RNA, herein designated VGAM RNA, to host target binding sites on VGAM971 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM971 host target RNA into VGAM971 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36263] It is appreciated that VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM971 host target genes. The mRNA of

each one of this plurality of VGAM971 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM971 RNA, herein designated VGAM RNA, and which when bound by VGAM971 RNA causes inhibition of translation of respective one or more VGAM971 host target proteins.

[36264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM971 gene, herein designated VGAM GENE, on one or more VGAM971 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[36265] It is yet further appreciated that a function of VGAM971 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM971 correlate with, and may be deduced from, the identity of the host target genes which VGAM971 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36266] Nucleotide sequences of the VGAM971 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM971 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM971 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM971 are further described hereinbelow with reference to Table 1.

[36267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM971 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM971 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[36268] As mentioned hereinabove with reference to Fig. 1, a function of VGAM971 gene, herein designated VGAM is inhibition of expression of VGAM971 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM971 correlate with, and may be deduced from, the identity of the target genes which VGAM971 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36269] Protein Tyrosine Phosphatase, Receptor Type, C (PTPRC, Accession NM_080923) is a VGAM971 host target gene. PTPRC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPRC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRC BINDING SITE, designated SEQ ID:28149, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36270] A function of VGAM971 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, C (PTPRC, Acces-

sion NM_080923). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRC. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155) is another VGAM971 host target gene. SERPINB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB9 BINDING SITE, designated SEQ ID:10366, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36271] Another function of VGAM971 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155), a gene which may be a serpin serine protease inhibitor that interacts with granzyme B (GZMB). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB9. The function of SERPINB9 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM60. Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600) is another VGAM971 host target gene. TCF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF3 BINDING SITE, designated SEQ ID:35006, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36272] Another function of VGAM971 is therefore inhibition of Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600), a gene which plays major roles in determining tissue-specific cell fate during embryogenesis. Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF3. The function of TCF3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM144.VAMP (vesicle-associated membrane protein)-associated Protein B and C (VAPB, Accession NM_004738) is another VGAM971 host target gene. VAPB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VAPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAPB BINDING SITE, designated SEQ ID:11132, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36273] Another function of VGAM971 is therefore inhibition of VAMP (vesicle-associated membrane protein)-associated Protein B and C (VAPB, Accession NM_004738). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAPB. DEPP (Accession NM_007021) is another VGAM971 host target gene. DEPP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DEPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEPP BINDING SITE,

designated SEQ ID:13877, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36274] Another function of VGAM971 is therefore inhibition of DEPP (Accession NM_007021). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEPP. DORFIN (Accession NM_015435) is another VGAM971 host target gene. DORFIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DORFIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DORFIN BINDING SITE, designated SEQ ID:17729, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36275] Another function of VGAM971 is therefore inhibition of DORFIN (Accession NM_015435). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DORFIN. KIAA1423 (Accession XM_029703) is another VGAM971 host target gene. KIAA1423 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by KIAA1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1423 BINDING SITE, designated SEQ ID:30923, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36276] Another function of VGAM971 is therefore inhibition of KIAA1423 (Accession XM_029703). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1423. Phospholipase C-like 2 (PLCL2, Accession XM_042836) is another VGAM971 host target gene. PLCL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLCL2 BINDING SITE, designated SEQ ID:33795, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36277] Another function of VGAM971 is therefore inhibition of

Phospholipase C-like 2 (PLCL2, Accession XM_042836). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLCL2. Splicing Factor, Arginine/serine-rich 11 (SFRS11, Accession NM_004768) is another VGAM971 host target gene. SFRS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS11 BINDING SITE, designated SEQ ID:11158, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36278] Another function of VGAM971 is therefore inhibition of Splicing Factor, Arginine/serine-rich 11 (SFRS11, Accession NM_004768). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS11. UBE3B (Accession XM_084941) is another VGAM971 host target gene. UBE3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE3B, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE3B BINDING SITE, designated SEQ ID:37775, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36279] Another function of VGAM971 is therefore inhibition of UBE3B (Accession XM_084941). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE3B. LOC155054 (Accession XM_088140) is another VGAM971 host target gene. LOC155054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155054 BINDING SITE, designated SEQ ID:39539, to the nucleotide sequence of VGAM971 RNA, herein designated VGAM RNA, also designated SEQ ID:3682.

[36280] Another function of VGAM971 is therefore inhibition of LOC155054 (Accession XM_088140). Accordingly, utilities of VGAM971 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC155054. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 972 (VGAM972) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36281] VGAM972 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM972 was detected is described hereinabove with reference to Figs. 1–8.

[36282] VGAM972 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36283] VGAM972 gene encodes a VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM972 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM972 precursor RNA is designated SEQ

ID:958, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:958 is located at position 53651 relative to the genome of *Melanoplus Sanguinipes* Entomopoxvirus.

[36284] VGAM972 precursor RNA folds onto itself, forming VGAM972 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36285] An enzyme complex designated DICER COMPLEX, `dices` the VGAM972 folded precursor RNA into VGAM972 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM972 RNA is designated SEQ ID:3683, and is provided hereinbelow with reference to the sequence

listing part.

[36286] VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM972 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36287] VGAM972 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM972 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM972 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36288] The complementary binding of VGAM972 RNA, herein designated VGAM RNA, to host target binding sites on VGAM972 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM972 host target RNA into VGAM972 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36289] It is appreciated that VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM972 host target genes. The mRNA of each one of this plurality of VGAM972 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM972 RNA, herein designated VGAM

RNA, and which when bound by VGAM972 RNA causes inhibition of translation of respective one or more VGAM972 host target proteins.

[36290] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM972 gene, herein designated VGAM GENE, on one or more VGAM972 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36291] It is yet further appreciated that a function of VGAM972 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM972 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM972 correlate with, and may be deduced from, the identity of the host target genes which VGAM972 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36292] Nucleotide sequences of the VGAM972 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM972 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM972 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM972 are further described hereinbelow with reference to Table 1.

[36293] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM972 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM972 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36294] As mentioned hereinabove with reference to Fig. 1, a function of VGAM972 gene, herein designated VGAM is

inhibition of expression of VGAM972 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM972 correlate with, and may be deduced from, the identity of the target genes which VGAM972 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36295] Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM_005670) is a VGAM972 host target gene. EPM2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPM2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPM2A BINDING SITE, designated SEQ ID:12225, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36296] A function of VGAM972 is therefore inhibition of Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM_005670), a gene which Laforin; protein tyrosine phosphatase that may have role in glycogen metabolism. Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with EPM2A. The function of EPM2A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM470. Kinesin-like 1 (KNSL1, Accession NM_004523) is another VGAM972 host target gene. KNSL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KNSL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KNSL1 BINDING SITE, designated SEQ ID:10863, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36297] Another function of VGAM972 is therefore inhibition of Kinesin-like 1 (KNSL1, Accession NM_004523), a gene which is a motor protein required for establishing a bipolar spindle. Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KNSL1. The function of KNSL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM252.BANP

(Accession XM_038696) is another VGAM972 host target gene. BANP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BANP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANP BINDING SITE, designated SEQ ID:32910, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36298] Another function of VGAM972 is therefore inhibition of BANP (Accession XM_038696). Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANP. GFR (Accession NM_012294) is another VGAM972 host target gene. GFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14645, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36299] Another function of VGAM972 is therefore inhibition of

GFR (Accession NM_012294). Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. Phytoceramidase, Alkaline (PHCA, Accession NM_018367) is another VGAM972 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20373, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36300] Another function of VGAM972 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM_018367). Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 10 (PSMD10, Accession NM_002814) is another VGAM972 host target gene. PSMD10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD10, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMD10 BINDING SITE, designated SEQ ID:8678, to the nucleotide sequence of VGAM972 RNA, herein designated VGAM RNA, also designated SEQ ID:3683.

[36301] Another function of VGAM972 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 10 (PSMD10, Accession NM_002814). Accordingly, utilities of VGAM972 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMD10. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 973 (VGAM973) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36302] VGAM973 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM973 was detected is described hereinabove with reference to Figs. 1-8.

[36303] VGAM973 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Equine Herpesvirus 1. VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36304] VGAM973 gene encodes a VGAM973 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM973 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM973 precursor RNA is designated SEQ ID:959, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:959 is located at position 96169 relative to the genome of Equine Herpesvirus 1.

[36305] VGAM973 precursor RNA folds onto itself, forming VGAM973 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36306] An enzyme complex designated DICER COMPLEX, `dices` the VGAM973 folded precursor RNA into VGAM973 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM973 RNA is designated SEQ ID:3684, and is provided hereinbelow with reference to the sequence listing part.

[36307] VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM973 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36308] VGAM973 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM973 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM973 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[36309] The complementary binding of VGAM973 RNA, herein designated VGAM RNA, to host target binding sites on VGAM973 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM973 host tar-

get RNA into VGAM973 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36310] It is appreciated that VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM973 host target genes. The mRNA of each one of this plurality of VGAM973 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM973 RNA, herein designated VGAM RNA, and which when bound by VGAM973 RNA causes inhibition of translation of respective one or more VGAM973 host target proteins.

[36311] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM973 gene, herein designated VGAM GENE, on one or more VGAM973 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36312] It is yet further appreciated that a function of VGAM973 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM973 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM973 correlate with, and may be deduced from, the identity of the host target genes which VGAM973 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36313] Nucleotide sequences of the VGAM973 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM973 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM973 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM973 are further

described hereinbelow with reference to Table 1.

[36314] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM973 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM973 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36315] As mentioned hereinabove with reference to Fig. 1, a function of VGAM973 gene, herein designated VGAM is inhibition of expression of VGAM973 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM973 correlate with, and may be deduced from, the identity of the target genes which VGAM973 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36316] Myxovirus (influenza virus) Resistance 1, Interferon-inducible Protein P78 (mouse) (MX1, Accession NM_002462) is a VGAM973 host target gene. MX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of MX1 BINDING SITE, designated SEQ ID:8291, to the nucleotide sequence of VGAM973 RNA, herein designated VGAM RNA, also designated SEQ ID:3684.

[36317] A function of VGAM973 is therefore inhibition of Myxovirus (influenza virus) Resistance 1, Interferon-inducible Protein P78 (mouse) (MX1, Accession NM_002462), a gene which is responsible for a specific antiviral state against influenza virus infection. Accordingly, utilities of VGAM973 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MX1. The function of MX1 has been established by previous studies. Horisberger et al. (1988) purified to homogeneity and characterized an interferon-induced human protein (p78 protein) that is the equivalent of the murine Mx1 protein as shown by antigenic relatedness, induction conditions, physicochemical properties, and amino acid analysis. The murine gene is located on chromosome 16. Horisberger et al. (1988) constructed a cDNA library using mRNAs from interferon-induced human diploid fibroblasts. They identified cDNA clones coding for the human p78 protein and used them to determine the chromosomal location of the corresponding gene, termed IFI-78K, by hybridization to

DNA from a panel of human–rodent somatic cell hybrids. The newly identified gene was located on human chromosome 21. Observation of a gene dosage effect with trisomic cells confirmed this location. The gene symbol MX, which corresponds to the mouse symbol Mx, is derived from myxovirus (influenza) resistance. Because Mx is the official title of this locus in the mouse, the same is used as the preferred symbol in man. There is a second MX gene on chromosome 21; thus, these are designated MX1 and MX2 (OMIM Ref. No. 147890). By somatic cell hybrid studies, Huber et al. (1988) likewise demonstrated that the 2 MX genes are located on distal mouse chromosome 16 and on human chromosome 21. By means of genetic linkage studies using RFLPs, Petersen et al. (1991) mapped the MX1 gene to 21q22.3 and determined its location relative to 15 other genes and DNA markers. Fanconi anemia (FA) consists of a group of at least 5 autosomal recessive disorders that share both clinical (e.g., birth defects and hematopoietic failure) and cellular (e.g., sensitivity to crosslinking agents and predisposition to apoptosis) features with each other. To identify genetic pathways that are altered in FA and to characterize shared molecular defects that might represent pathogenetic links

among these groups, Li and Youssoufian (1997) used mRNA differential display to isolate the genes that have altered expression patterns in FA cells. They reported that the expression of an interferon-inducible gene, which they referred to as MxA, is highly upregulated in cells of FA complementation groups A, B, C, and D, but that it is suppressed in FA group C cells (OMIM Ref. No. 227645) complemented with wildtype FAC cDNA, as well as in non-FA cells. A posttranslational mechanism rather than transcriptional induction appeared to account for MxA overexpression. Forced expression of MxA in Hep3B cells enhanced their sensitivity to mitomycin C and induced apoptosis, similar to the FA phenotype. Thus, MxA is a downstream target of FAC and is the first genetic marker to be identified among multiple FA complementation groups. FA subtypes may converge onto a final common pathway, which is intimately related to the interferon signaling mechanism. Constitutive activity of this pathway may explain a number of the phenotypic features of FA, particularly the pathogenesis of bone marrow failure.

[36318] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [36319] Horisberger, M. A.; Wathelet, M.; Szpirer, J.; Szpirer, C.; Islam, Q.; Levan, G.; Huez, G.; Content, J. : cDNA cloning and assignment to chromosome 21 of IFI-78K gene, the human equivalent of murine Mx gene. *Somat. Cell Molec. Genet.* 14: 123–131, 1988. ; and
- [36320] Li, Y.; Youssoufian, H. : MxA overexpression reveals a common genetic link in four Fanconi anemia complementation groups. *J. Clin. Invest.* 100: 2873–2880, 1997.
- [36321] Further studies establishing the function and utilities of MX1 are found in John Hopkins OMIM database record ID 147150, and in cited publications numbered 2019–2021, 496 and 12304 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM_002384) is another VGAM973 host target gene. DGKD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKD BINDING SITE, designated SEQ ID:29878, to the nucleotide sequence of VGAM973 RNA, herein designated VGAM RNA, also designated SEQ ID:3684.

[36322] Another function of VGAM973 is therefore inhibition of Diacylglycerol Kinase, Delta 130kDa (DGKD, Accession XM_002384). Accordingly, utilities of VGAM973 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKD. LOC201696 (Accession XM_032269) is another VGAM973 host target gene. LOC201696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201696 BINDING SITE, designated SEQ ID:31623, to the nucleotide sequence of VGAM973 RNA, herein designated VGAM RNA, also designated SEQ ID:3684.

[36323] Another function of VGAM973 is therefore inhibition of LOC201696 (Accession XM_032269). Accordingly, utilities of VGAM973 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 974 (VGAM974) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36324] VGAM974 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM974 was detected is described hereinabove with reference to Figs. 1–8.

[36325] VGAM974 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36326] VGAM974 gene encodes a VGAM974 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM974 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM974 precursor RNA is designated SEQ ID:960, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:960 is located at position 142776 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[36327] VGAM974 precursor RNA folds onto itself, forming

VGAM974 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36328] An enzyme complex designated DICER COMPLEX, `dices` the VGAM974 folded precursor RNA into VGAM974 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM974 RNA is designated SEQ ID:3685, and is provided hereinbelow with reference to the sequence listing part.

[36329] VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM974 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36330] VGAM974 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM974 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM974 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36331] The complementary binding of VGAM974 RNA, herein designated VGAM RNA, to host target binding sites on VGAM974 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM974 host target RNA into VGAM974 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36332] It is appreciated that VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM974 host target genes. The mRNA of each one of this plurality of VGAM974 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM974 RNA, herein designated VGAM RNA, and which when bound by VGAM974 RNA causes inhibition of translation of respective one or more VGAM974 host target proteins.

[36333] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM974 gene, herein designated VGAM GENE, on one or more VGAM974 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36334] It is yet further appreciated that a function of VGAM974 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM974 correlate with, and may be deduced from, the identity of the host target genes which VGAM974

binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36335] Nucleotide sequences of the VGAM974 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM974 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM974 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM974 are further described hereinbelow with reference to Table 1.

[36336] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM974 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM974 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36337] As mentioned hereinabove with reference to Fig. 1, a function of VGAM974 gene, herein designated VGAM is inhibition of expression of VGAM974 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM974 correlate with, and may be deduced from, the identity of the target genes which VGAM974 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[36338] Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862) is a VGAM974 host target gene. ARNT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNT2 BINDING SITE, designated SEQ ID:16932, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36339] A function of VGAM974 is therefore inhibition of Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862), a gene which specifically recognizes the xenobiotic response element (xre). Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNT2. The function of ARNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275) is another

VGAM974 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14594, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36340] Another function of VGAM974 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263. Protein Tyrosine Phosphatase, Non-receptor Type 1 (PTPN1, Accession NM_002827) is another VGAM974 host target gene. PTPN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPN1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPN1 BINDING SITE, designated SEQ ID:8702, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36341] Another function of VGAM974 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type 1 (PTPN1, Accession NM_002827), a gene which is a non-receptor type 1 protein tyrosine phosphatase and inhibits insulin signaling. Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPN1. The function of PTPN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM327. Transcription Factor 19 (SC1) (TCF19, Accession XM_175167) is another VGAM974 host target gene. TCF19 BINDING SITE1 and TCF19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of TCF19 BINDING SITE1 and TCF19 BINDING SITE2, designated SEQ ID:46656 and SEQ ID:46705 respectively, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36342] Another function of VGAM974 is therefore inhibition of Transcription Factor 19 (SC1) (TCF19, Accession XM_175167), a gene which plays an important role in the transcription of genes required for the later stages of cell cycle progression. Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF19. The function of TCF19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM299.KIAA0461 (Accession XM_047883) is another VGAM974 host target gene. KIAA0461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0461 BINDING SITE, designated SEQ ID:35071, to the

nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36343] Another function of VGAM974 is therefore inhibition of KIAA0461 (Accession XM_047883). Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0461. LOC200597 (Accession XM_114266) is another VGAM974 host target gene. LOC200597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200597 BINDING SITE, designated SEQ ID:42823, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36344] Another function of VGAM974 is therefore inhibition of LOC200597 (Accession XM_114266). Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200597. LOC220522 (Accession XM_018306) is another VGAM974 host target gene. LOC220522 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220522 BINDING SITE, designated SEQ ID:30354, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36345] Another function of VGAM974 is therefore inhibition of LOC220522 (Accession XM_018306). Accordingly, utilities of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220522. LOC257319 (Accession XM_171049) is another VGAM974 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45829, to the nucleotide sequence of VGAM974 RNA, herein designated VGAM RNA, also designated SEQ ID:3685.

[36346] Another function of VGAM974 is therefore inhibition of LOC257319 (Accession XM_171049). Accordingly, utilities

of VGAM974 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 975 (VGAM975) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36347] VGAM975 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM975 was detected is described hereinabove with reference to Figs. 1–8.

[36348] VGAM975 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36349] VGAM975 gene encodes a VGAM975 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM975 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM975 precursor RNA is designated SEQ

ID:961, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:961 is located at position 34911 relative to the genome of Variola Virus.

[36350] VGAM975 precursor RNA folds onto itself, forming VGAM975 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36351] An enzyme complex designated DICER COMPLEX, `dices` the VGAM975 folded precursor RNA into VGAM975 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM975 RNA is designated SEQ ID:3686, and is provided hereinbelow with reference to the sequence

listing part.

[36352] VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM975 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36353] VGAM975 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM975 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM975 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36354] The complementary binding of VGAM975 RNA, herein designated VGAM RNA, to host target binding sites on VGAM975 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM975 host target RNA into VGAM975 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36355] It is appreciated that VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM975 host target genes. The mRNA of each one of this plurality of VGAM975 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM975 RNA, herein designated VGAM

RNA, and which when bound by VGAM975 RNA causes inhibition of translation of respective one or more VGAM975 host target proteins.

[36356] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM975 gene, herein designated VGAM GENE, on one or more VGAM975 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36357] It is yet further appreciated that a function of VGAM975 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM975 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM975 correlate with, and may be deduced from, the identity of the host target genes which VGAM975 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36358] Nucleotide sequences of the VGAM975 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM975 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM975 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM975 are further described hereinbelow with reference to Table 1.

[36359] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM975 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM975 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36360] As mentioned hereinabove with reference to Fig. 1, a function of VGAM975 gene, herein designated VGAM is

inhibition of expression of VGAM975 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM975 correlate with, and may be deduced from, the identity of the target genes which VGAM975 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36361] Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM_054111) is a VGAM975 host target gene. IHPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK3 BINDING SITE, designated SEQ ID:27654, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36362] A function of VGAM975 is therefore inhibition of Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM_054111). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK3. DKFZP434D193 (Accession XM_114297) is another VGAM975 host target gene. DKFZP434D193 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by DKFZP434D193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434D193 BINDING SITE, designated SEQ ID:42852, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36363] Another function of VGAM975 is therefore inhibition of DKFZP434D193 (Accession XM_114297). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434D193. Fucose-1-phosphate Guanylyltransferase (FPGT, Accession NM_003838) is another VGAM975 host target gene. FPGT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FPGT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FPGT BINDING SITE, designated SEQ ID:9929, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36364] Another function of VGAM975 is therefore inhibition of Fucose-1-phosphate Guanylyltransferase (FPGT, Accession NM_003838). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FPGT. KIAA0252 (Accession XM_031646) is another VGAM975 host target gene. KIAA0252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0252 BINDING SITE, designated SEQ ID:31449, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36365] Another function of VGAM975 is therefore inhibition of KIAA0252 (Accession XM_031646). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0252. Mal, T-cell Differentiation Protein 2 (MAL2, Accession NM_052886) is another VGAM975 host target gene. MAL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAL2 BINDING SITE, designated SEQ ID:27467, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36366] Another function of VGAM975 is therefore inhibition of Mal, T-cell Differentiation Protein 2 (MAL2, Accession NM_052886). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAL2. LOC122553 (Accession XM_058630) is another VGAM975 host target gene. LOC122553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122553 BINDING SITE, designated SEQ ID:36687, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36367] Another function of VGAM975 is therefore inhibition of LOC122553 (Accession XM_058630). Accordingly, utilities

of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122553. LOC170425 (Accession XM_084330) is another VGAM975 host target gene. LOC170425 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170425 BINDING SITE, designated SEQ ID:37548, to the nucleotide sequence of VGAM975 RNA, herein designated VGAM RNA, also designated SEQ ID:3686.

[36368] Another function of VGAM975 is therefore inhibition of LOC170425 (Accession XM_084330). Accordingly, utilities of VGAM975 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170425. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 976 (VGAM976) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36369] VGAM976 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM976 was detected is described hereinabove with reference to Figs. 1–8.

[36370] VGAM976 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36371] VGAM976 gene encodes a VGAM976 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM976 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM976 precursor RNA is designated SEQ ID:962, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:962 is located at position 48892 relative to the genome of Camelpox Virus.

[36372] VGAM976 precursor RNA folds onto itself, forming VGAM976 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36373] An enzyme complex designated DICER COMPLEX, `dices` the VGAM976 folded precursor RNA into VGAM976 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 69%) nucleotide sequence of VGAM976 RNA is designated SEQ ID:3687, and is provided hereinbelow with reference to the sequence listing part.

[36374] VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM976 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[36375] VGAM976 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM976 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM976 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36376] The complementary binding of VGAM976 RNA, herein designated VGAM RNA, to host target binding sites on VGAM976 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM976 host target RNA into VGAM976 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36377] It is appreciated that VGAM976 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM976 host target genes. The mRNA of each one of this plurality of VGAM976 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM976 RNA, herein designated VGAM RNA, and which when bound by VGAM976 RNA causes inhibition of translation of respective one or more VGAM976 host target proteins.

[36378] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM976 gene, herein designated VGAM GENE, on one or more VGAM976 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36379] It is yet further appreciated that a function of VGAM976 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM976 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM976 correlate with, and may be deduced from, the identity of the host target genes which VGAM976 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36380] Nucleotide sequences of the VGAM976 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM976 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM976 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM976 are further
described hereinbelow with reference to Table 1.

[36381] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM976 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM976 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[36382] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM976 gene, herein designated VGAM is
inhibition of expression of VGAM976 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM976 correlate with, and may be deduced
from, the identity of the target genes which VGAM976
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[36383] Fibronectin Leucine Rich Transmembrane Protein 2
(FLRT2, Accession NM_013231) is a VGAM976 host target

gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14877, to the nucleotide sequence of VGAM976 RNA, herein designated VGAM RNA, also designated SEQ ID:3687.

[36384] A function of VGAM976 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM976 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.KIAA1468 (Accession XM_166289) is another VGAM976 host target gene. KIAA1468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1468, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1468 BINDING SITE, designated SEQ ID:44097, to the nucleotide sequence of VGAM976 RNA, herein designated VGAM RNA, also designated SEQ ID:3687.

[36385] Another function of VGAM976 is therefore inhibition of KIAA1468 (Accession XM_166289). Accordingly, utilities of VGAM976 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1468. KIAA1979 (Accession XM_113984) is another VGAM976 host target gene. KIAA1979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1979 BINDING SITE, designated SEQ ID:42588, to the nucleotide sequence of VGAM976 RNA, herein designated VGAM RNA, also designated SEQ ID:3687.

[36386] Another function of VGAM976 is therefore inhibition of KIAA1979 (Accession XM_113984). Accordingly, utilities of VGAM976 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 977 (VGAM977) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36387] VGAM977 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM977 was detected is described hereinabove with reference to Figs. 1–8.

[36388] VGAM977 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36389] VGAM977 gene encodes a VGAM977 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM977 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM977 precursor RNA is designated SEQ ID:963, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:963 is

located at position 38963 relative to the genome of Vari-
ola Virus.

[36390] VGAM977 precursor RNA folds onto itself, forming VGAM977 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36391] An enzyme complex designated DICER COMPLEX, `dices` the VGAM977 folded precursor RNA into VGAM977 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM977 RNA is designated SEQ ID:3688, and is provided hereinbelow with reference to the sequence listing part.

[36392] VGAM977 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM977 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[36393] VGAM977 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM977 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM977 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM977 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36394] The complementary binding of VGAM977 RNA, herein designated VGAM RNA, to host target binding sites on VGAM977 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM977 host target RNA into VGAM977 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36395] It is appreciated that VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM977 host target genes. The mRNA of each one of this plurality of VGAM977 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM977 RNA, herein designated VGAM RNA, and which when bound by VGAM977 RNA causes inhibition of translation of respective one or more VGAM977

host target proteins.

[36396] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM977 gene, herein designated VGAM GENE, on one or more VGAM977 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36397] It is yet further appreciated that a function of VGAM977 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific func-

tions, and accordingly utilities, of VGAM977 correlate with, and may be deduced from, the identity of the host target genes which VGAM977 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36398] Nucleotide sequences of the VGAM977 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM977 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM977 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM977 are further described hereinbelow with reference to Table 1.

[36399] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM977 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM977 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36400] As mentioned hereinabove with reference to Fig. 1, a function of VGAM977 gene, herein designated VGAM is inhibition of expression of VGAM977 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM977 correlate with, and may be deduced from, the identity of the target genes which VGAM977 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36401] HIS1 (Accession NM_006460) is a VGAM977 host target gene. HIS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIS1 BINDING SITE, designated SEQ ID:13179, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36402] A function of VGAM977 is therefore inhibition of HIS1 (Accession NM_006460). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIS1. Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223) is another VGAM977 host target gene. ITPR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of ITPR2 BINDING SITE, designated SEQ ID:7992, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36403] Another function of VGAM977 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR2. KIAA0342 (Accession XM_047357) is another VGAM977 host target gene. KIAA0342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0342 BINDING SITE, designated SEQ ID:34960, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36404] Another function of VGAM977 is therefore inhibition of KIAA0342 (Accession XM_047357). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0342. KIAA1948 (Accession XM_091984) is another VGAM977 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40083, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36405] Another function of VGAM977 is therefore inhibition of KIAA1948 (Accession XM_091984). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1948. MAC30 (Accession XM_031536) is another VGAM977 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAC30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ ID:31404, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA,

also designated SEQ ID:3688.

[36406] Another function of VGAM977 is therefore inhibition of MAC30 (Accession XM_031536). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. MY014 (Accession NM_030918) is another VGAM977 host target gene. MY014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MY014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MY014 BINDING SITE, designated SEQ ID:25189, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36407] Another function of VGAM977 is therefore inhibition of MY014 (Accession NM_030918). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MY014. LOC158056 (Accession XM_088463) is another VGAM977 host target gene. LOC158056 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158056, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158056 BINDING SITE, designated SEQ ID:39713, to the nucleotide sequence of VGAM977 RNA, herein designated VGAM RNA, also designated SEQ ID:3688.

[36408] Another function of VGAM977 is therefore inhibition of LOC158056 (Accession XM_088463). Accordingly, utilities of VGAM977 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158056. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 978 (VGAM978) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36409] VGAM978 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM978 was detected is described hereinabove with reference to Figs. 1–8.

[36410] VGAM978 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36411] VGAM978 gene encodes a VGAM978 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM978 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM978 precursor RNA is designated SEQ ID:964, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:964 is located at position 55420 relative to the genome of Ectromelia Virus.

[36412] VGAM978 precursor RNA folds onto itself, forming VGAM978 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36413] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM978 folded precursor RNA into VGAM978 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM978 RNA is designated SEQ ID:3689, and is provided hereinbelow with reference to the sequence listing part.

[36414] VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM978 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36415] VGAM978 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM978 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM978 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36416] The complementary binding of VGAM978 RNA, herein designated VGAM RNA, to host target binding sites on VGAM978 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM978 host target RNA into VGAM978 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36417] It is appreciated that VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM978 host target genes. The mRNA of each one of this plurality of VGAM978 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM978 RNA, herein designated VGAM RNA, and which when bound by VGAM978 RNA causes inhibition of translation of respective one or more VGAM978 host target proteins.

[36418] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM978 gene, herein designated VGAM GENE, on one or more VGAM978 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36419] It is yet further appreciated that a function of VGAM978 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM978 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM978 correlate with, and may be deduced from, the identity of the host target genes which VGAM978 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36420] Nucleotide sequences of the VGAM978 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM978 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM978 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM978 are further described hereinbelow with reference to Table 1.

[36421] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM978 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM978 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36422] As mentioned hereinabove with reference to Fig. 1, a function of VGAM978 gene, herein designated VGAM is inhibition of expression of VGAM978 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM978 correlate with, and may be deduced from, the identity of the target genes which VGAM978 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36423] FLJ12806 (Accession NM_022831) is a VGAM978 host target gene. FLJ12806 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12806 BINDING SITE, designated SEQ ID:23110, to the nucleotide sequence of VGAM978

RNA, herein designated VGAM RNA, also designated SEQ ID:3689.

[36424] A function of VGAM978 is therefore inhibition of FLJ12806 (Accession NM_022831). Accordingly, utilities of VGAM978 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12806. LOC157621 (Accession XM_098800) is another VGAM978 host target gene. LOC157621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157621 BINDING SITE, designated SEQ ID:41824, to the nucleotide sequence of VGAM978 RNA, herein designated VGAM RNA, also designated SEQ ID:3689.

[36425] Another function of VGAM978 is therefore inhibition of LOC157621 (Accession XM_098800). Accordingly, utilities of VGAM978 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157621. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 979 (VGAM979) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36426] VGAM979 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM979 was detected is described hereinabove with reference to Figs. 1–8.

[36427] VGAM979 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36428] VGAM979 gene encodes a VGAM979 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM979 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM979 precursor RNA is designated SEQ ID:965, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:965 is located at position 50081 relative to the genome of Camelpox Virus.

[36429] VGAM979 precursor RNA folds onto itself, forming VGAM979 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36430] An enzyme complex designated DICER COMPLEX, `dices` the VGAM979 folded precursor RNA into VGAM979 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM979 RNA is designated SEQ ID:3690, and is provided hereinbelow with reference to the sequence listing part.

[36431] VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM979 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM979 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36432] VGAM979 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM979 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM979 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36433] The complementary binding of VGAM979 RNA, herein designated VGAM RNA, to host target binding sites on VGAM979 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM979 host target RNA into VGAM979 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36434] It is appreciated that VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM979 host target genes. The mRNA of each one of this plurality of VGAM979 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM979 RNA, herein designated VGAM RNA, and which when bound by VGAM979 RNA causes inhibition of translation of respective one or more VGAM979 host target proteins.

[36435] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM979 gene, herein designated VGAM GENE, on one or more VGAM979 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36436] It is yet further appreciated that a function of VGAM979 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM979 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM979 correlate with, and may be deduced from, the identity of the host

target genes which VGAM979 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36437] Nucleotide sequences of the VGAM979 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM979 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM979 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM979 are further described hereinbelow with reference to Table 1.

[36438] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM979 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM979 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36439] As mentioned hereinabove with reference to Fig. 1, a function of VGAM979 gene, herein designated VGAM is inhibition of expression of VGAM979 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM979 correlate with, and may be deduced from, the identity of the target genes which VGAM979

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36440] ACF (Accession NM_014576) is a VGAM979 host target gene. ACF BINDING SITE1 and ACF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACF, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACF BINDING SITE1 and ACF BINDING SITE2, designated SEQ ID:15937 and SEQ ID:29058 respectively, to the nucleotide sequence of VGAM979 RNA, herein designated VGAM RNA, also designated SEQ ID:3690.

[36441] A function of VGAM979 is therefore inhibition of ACF (Accession NM_014576). Accordingly, utilities of VGAM979 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACF. p21(CDKN1A)-activated Kinase 7 (PAK7, Accession XM_045653) is another VGAM979 host target gene. PAK7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PAK7 BINDING SITE, designated SEQ ID:34507, to the nucleotide sequence of VGAM979 RNA, herein designated VGAM RNA, also designated SEQ ID:3690.

[36442] Another function of VGAM979 is therefore inhibition of p21(CDKN1A)–activated Kinase 7 (PAK7, Accession XM_045653). Accordingly, utilities of VGAM979 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK7. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 980 (VGAM980) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36443] VGAM980 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM980 was detected is described hereinabove with reference to Figs. 1–8.

[36444] VGAM980 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[36445] VGAM980 gene encodes a VGAM980 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM980 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM980 precursor RNA is designated SEQ ID:966, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:966 is located at position 54779 relative to the genome of Ectromelia Virus.

[36446] VGAM980 precursor RNA folds onto itself, forming VGAM980 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36447] An enzyme complex designated DICER COMPLEX, `dices` the VGAM980 folded precursor RNA into VGAM980 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 69%) nucleotide sequence of VGAM980 RNA is designated SEQ ID:3691, and is provided hereinbelow with reference to the sequence listing part.

[36448] VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM980 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36449] VGAM980 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM980 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM980 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36450] The complementary binding of VGAM980 RNA, herein designated VGAM RNA, to host target binding sites on VGAM980 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM980 host target RNA into VGAM980 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36451] It is appreciated that VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM980 host target genes. The mRNA of each one of this plurality of VGAM980 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM980 RNA, herein designated VGAM RNA, and which when bound by VGAM980 RNA causes inhibition of translation of respective one or more VGAM980 host target proteins.

[36452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM980 gene, herein designated VGAM GENE, on one or more VGAM980 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36453] It is yet further appreciated that a function of VGAM980 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM980 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM980 correlate with, and may be deduced from, the identity of the host target genes which VGAM980 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36454] Nucleotide sequences of the VGAM980 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM980 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM980 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM980 are further described hereinbelow with reference to Table 1.

[36455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM980 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM980 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36456] As mentioned hereinabove with reference to Fig. 1, a function of VGAM980 gene, herein designated VGAM is inhibition of expression of VGAM980 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM980 correlate with, and may be deduced from, the identity of the target genes which VGAM980 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36457] Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is a VGAM980 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14877, to the nucleotide sequence of VGAM980 RNA, herein designated VGAM RNA, also designated SEQ

ID:3691.

[36458] A function of VGAM980 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM980 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.KIAA1468 (Accession XM_166289) is another VGAM980 host target gene. KIAA1468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1468 BINDING SITE, designated SEQ ID:44097, to the nucleotide sequence of VGAM980 RNA, herein designated VGAM RNA, also designated SEQ ID:3691.

[36459] Another function of VGAM980 is therefore inhibition of KIAA1468 (Accession XM_166289). Accordingly, utilities of VGAM980 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1468. KIAA1979 (Accession XM_113984) is another VGAM980 host target gene. KIAA1979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1979 BINDING SITE, designated SEQ ID:42588, to the nucleotide sequence of VGAM980 RNA, herein designated VGAM RNA, also designated SEQ ID:3691.

[36460] Another function of VGAM980 is therefore inhibition of KIAA1979 (Accession XM_113984). Accordingly, utilities of VGAM980 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 981 (VGAM981) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36461] VGAM981 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM981 was detected is described hereinabove with reference to Figs. 1–8.

[36462] VGAM981 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36463] VGAM981 gene encodes a VGAM981 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM981 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM981 precursor RNA is designated SEQ ID:967, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:967 is located at position 62393 relative to the genome of Cowpox Virus.

[36464] VGAM981 precursor RNA folds onto itself, forming VGAM981 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36465] An enzyme complex designated DICER COMPLEX, `dices` the VGAM981 folded precursor RNA into VGAM981 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM981 RNA is designated SEQ ID:3692, and is provided hereinbelow with reference to the sequence listing part.

[36466] VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM981 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36467] VGAM981 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM981 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM981 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36468] The complementary binding of VGAM981 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM981 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM981 host target RNA into VGAM981 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36469] It is appreciated that VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM981 host target genes. The mRNA of each one of this plurality of VGAM981 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM981 RNA, herein designated VGAM RNA, and which when bound by VGAM981 RNA causes inhibition of translation of respective one or more VGAM981 host target proteins.

[36470] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM981 gene, herein designated VGAM GENE, on one or more VGAM981 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36471] It is yet further appreciated that a function of VGAM981 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM981 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM981 correlate with, and may be deduced from, the identity of the host target genes which VGAM981 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36472] Nucleotide sequences of the VGAM981 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM981 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM981 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM981 are further described hereinbelow with reference to Table 1.

[36473] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM981 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM981 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36474] As mentioned hereinabove with reference to Fig. 1, a function of VGAM981 gene, herein designated VGAM is inhibition of expression of VGAM981 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM981 correlate with, and may be deduced from, the identity of the target genes which VGAM981 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36475] DKFZp761O0113 (Accession NM_018409) is a VGAM981 host target gene. DKFZp761O0113 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region

of mRNA encoded by DKFZp761O0113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761O0113 BINDING SITE, designated SEQ ID:20446, to the nucleotide sequence of VGAM981 RNA, herein designated VGAM RNA, also designated SEQ ID:3692.

[36476] A function of VGAM981 is therefore inhibition of DKFZp761O0113 (Accession NM_018409). Accordingly, utilities of VGAM981 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761O0113. KIAA1084 (Accession NM_014910) is another VGAM981 host target gene. KIAA1084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1084 BINDING SITE, designated SEQ ID:17136, to the nucleotide sequence of VGAM981 RNA, herein designated VGAM RNA, also designated SEQ ID:3692.

[36477] Another function of VGAM981 is therefore inhibition of KIAA1084 (Accession NM_014910). Accordingly, utilities

of VGAM981 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1084. LOC158629 (Accession XM_098972) is another VGAM981 host target gene. LOC158629 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158629, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158629 BINDING SITE, designated SEQ ID:42021, to the nucleotide sequence of VGAM981 RNA, herein designated VGAM RNA, also designated SEQ ID:3692.

[36478] Another function of VGAM981 is therefore inhibition of LOC158629 (Accession XM_098972). Accordingly, utilities of VGAM981 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158629. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 982 (VGAM982) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36479] VGAM982 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM982 was detected is described hereinabove with reference to Figs. 1–8.

[36480] VGAM982 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36481] VGAM982 gene encodes a VGAM982 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM982 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM982 precursor RNA is designated SEQ ID:968, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:968 is located at position 54629 relative to the genome of Ectromelia Virus.

[36482] VGAM982 precursor RNA folds onto itself, forming VGAM982 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36483] An enzyme complex designated DICER COMPLEX, `dices` the VGAM982 folded precursor RNA into VGAM982 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM982 RNA is designated SEQ ID:3693, and is provided hereinbelow with reference to the sequence listing part.

[36484] VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM982 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[36485] VGAM982 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM982 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM982 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36486] The complementary binding of VGAM982 RNA, herein designated VGAM RNA, to host target binding sites on VGAM982 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM982 host target RNA into VGAM982 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36487] It is appreciated that VGAM982 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM982 host target genes. The mRNA of each one of this plurality of VGAM982 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM982 RNA, herein designated VGAM RNA, and which when bound by VGAM982 RNA causes inhibition of translation of respective one or more VGAM982 host target proteins.

[36488] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM982 gene, herein designated VGAM GENE, on one or more VGAM982 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36489] It is yet further appreciated that a function of VGAM982 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM982 correlate with, and may be deduced from, the identity of the host target genes which VGAM982 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36490] Nucleotide sequences of the VGAM982 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM982 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM982 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM982 are further
described hereinbelow with reference to Table 1.

[36491] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM982 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM982 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[36492] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM982 gene, herein designated VGAM is
inhibition of expression of VGAM982 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM982 correlate with, and may be deduced
from, the identity of the target genes which VGAM982
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[36493] Leucine Zipper-EF-hand Containing Transmembrane Pro-
tein 1 (LETM1, Accession NM_012318) is a VGAM982 host

target gene. LETM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LETM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LETM1 BINDING SITE, designated SEQ ID:14696, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36494] A function of VGAM982 is therefore inhibition of Leucine Zipper-EF-hand Containing Transmembrane Protein 1 (LETM1, Accession NM_012318). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LETM1. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_002848) is another VGAM982 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ

ID:8737, SEQ ID:25002, SEQ ID:25008, SEQ ID:25017 and SEQ ID:25026 respectively, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36495] Another function of VGAM982 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_002848), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM982 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15355, to the nucleotide sequence of VGAM982 RNA,

herein designated VGAM RNA, also designated SEQ ID:3693.

[36496] Another function of VGAM982 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726) is another VGAM982 host target gene. ABCC13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC13 BINDING SITE, designated SEQ ID:28973, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36497] Another function of VGAM982 is therefore inhibition of

ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC13. Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM_025225) is another VGAM982 host target gene. C22orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf20 BINDING SITE, designated SEQ ID:24901, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36498] Another function of VGAM982 is therefore inhibition of Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM_025225). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf20. FLJ12056 (Accession NM_024933) is another VGAM982 host target gene. FLJ12056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ12056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12056 BINDING SITE, designated SEQ ID:24469, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36499] Another function of VGAM982 is therefore inhibition of FLJ12056 (Accession NM_024933). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12056. FLJ30681 (Accession XM_166291) is another VGAM982 host target gene. FLJ30681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30681 BINDING SITE, designated SEQ ID:44105, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36500] Another function of VGAM982 is therefore inhibition of FLJ30681 (Accession XM_166291). Accordingly, utilities of

VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30681. HSA249128 (Accession NM_017583) is another VGAM982 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19028, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36501] Another function of VGAM982 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA249128. KIAA0774 (Accession XM_166270) is another VGAM982 host target gene. KIAA0774 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0774, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0774 BINDING SITE, designated SEQ ID:44087, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36502] Another function of VGAM982 is therefore inhibition of KIAA0774 (Accession XM_166270). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0774. KIAA1867 (Accession XM_170675) is another VGAM982 host target gene. KIAA1867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1867 BINDING SITE, designated SEQ ID:45456, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36503] Another function of VGAM982 is therefore inhibition of KIAA1867 (Accession XM_170675). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1867. LAP1B (Accession XM_035429) is another VGAM982 host target gene. LAP1B BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by LAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAP1B BINDING SITE, designated SEQ ID:32264, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36504] Another function of VGAM982 is therefore inhibition of LAP1B (Accession XM_035429). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAP1B. MGC4796 (Accession XM_029031) is another VGAM982 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30827, to the nucleotide sequence of VGAM982 RNA, herein designated VGAM RNA, also designated SEQ ID:3693.

[36505] Another function of VGAM982 is therefore inhibition of

MGC4796 (Accession XM_029031). Accordingly, utilities of VGAM982 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 983 (VGAM983) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36506] VGAM983 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM983 was detected is described hereinabove with reference to Figs. 1–8.

[36507] VGAM983 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus. VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36508] VGAM983 gene encodes a VGAM983 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM983 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM983 precursor RNA is designated SEQ ID:969, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:969 is located at position 54050 relative to the genome of Ectromelia Virus.

[36509] VGAM983 precursor RNA folds onto itself, forming VGAM983 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36510] An enzyme complex designated DICER COMPLEX, `dices` the VGAM983 folded precursor RNA into VGAM983 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM983 RNA is designated SEQ ID:3694, and is provided hereinbelow with reference to the sequence listing part.

[36511] VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM983 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[36512] VGAM983 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM983 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM983 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[36513] The complementary binding of VGAM983 RNA, herein designated VGAM RNA, to host target binding sites on VGAM983 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM983 host target RNA into VGAM983 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36514] It is appreciated that VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM983 host target genes. The mRNA of each one of this plurality of VGAM983 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM983 RNA, herein designated VGAM RNA, and which when bound by VGAM983 RNA causes inhibition of translation of respective one or more VGAM983 host target proteins.

[36515] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM983 gene, herein designated VGAM GENE, on one or more VGAM983 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36516] It is yet further appreciated that a function of VGAM983 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM983 correlate with, and may be deduced from, the identity of the host target genes which VGAM983 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[36517] Nucleotide sequences of the VGAM983 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM983 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM983 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM983 are further described hereinbelow with reference to Table 1.

[36518] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM983 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM983 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36519] As mentioned hereinabove with reference to Fig. 1, a function of VGAM983 gene, herein designated VGAM is inhibition of expression of VGAM983 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM983 correlate with, and may be deduced from, the identity of the target genes which VGAM983 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36520] Sulfotransferase Family, Cytosolic, 1C, Member 1 (SULT1C1, Accession NM_001056) is a VGAM983 host target gene. SULT1C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SULT1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT1C1 BINDING SITE, designated SEQ ID:6718, to the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, also designated SEQ ID:3694.

[36521] A function of VGAM983 is therefore inhibition of Sulfotransferase Family, Cytosolic, 1C, Member 1 (SULT1C1, Accession NM_001056). Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with SULT1C1. Chromosome X Open Reading Frame 1 (CXorf1, Accession NM_004709) is another VGAM983 host target gene. CXorf1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CXorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf1 BINDING SITE, designated SEQ ID:11052, to the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, also designated SEQ ID:3694.

[36522] Another function of VGAM983 is therefore inhibition of Chromosome X Open Reading Frame 1 (CXorf1, Accession NM_004709). Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf1. KIAA1211 (Accession XM_044178) is another VGAM983 host target gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of KIAA1211 BINDING SITE, designated SEQ ID:34164, to the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, also designated SEQ ID:3694.

[36523] Another function of VGAM983 is therefore inhibition of KIAA1211 (Accession XM_044178). Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373) is another VGAM983 host target gene. SH3BGRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL BINDING SITE, designated SEQ ID:31022, to the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, also designated SEQ ID:3694.

[36524] Another function of VGAM983 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373). Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SH3BGRL. LOC221143 (Accession XM_167986) is another VGAM983 host target gene. LOC221143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221143 BINDING SITE, designated SEQ ID:44940, to the nucleotide sequence of VGAM983 RNA, herein designated VGAM RNA, also designated SEQ ID:3694.

[36525] Another function of VGAM983 is therefore inhibition of LOC221143 (Accession XM_167986). Accordingly, utilities of VGAM983 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221143. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 984 (VGAM984) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36526] VGAM984 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM984 was detected is described hereinabove with reference to Figs. 1–8.

[36527] VGAM984 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36528] VGAM984 gene encodes a VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM984 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM984 precursor RNA is designated SEQ ID:970, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:970 is located at position 64055 relative to the genome of Cowpox Virus.

[36529] VGAM984 precursor RNA folds onto itself, forming VGAM984 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36530] An enzyme complex designated DICER COMPLEX, `dices` the VGAM984 folded precursor RNA into VGAM984 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM984 RNA is designated SEQ ID:3695, and is provided hereinbelow with reference to the sequence listing part.

[36531] VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM984 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36532] VGAM984 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM984 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM984 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36533] The complementary binding of VGAM984 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM984 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM984 host target RNA into VGAM984 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36534] It is appreciated that VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM984 host target genes. The mRNA of each one of this plurality of VGAM984 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM984 RNA, herein designated VGAM RNA, and which when bound by VGAM984 RNA causes inhibition of translation of respective one or more VGAM984 host target proteins.

[36535] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM984 gene, herein designated VGAM GENE, on one or more VGAM984 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36536] It is yet further appreciated that a function of VGAM984 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM984 correlate with, and may be deduced from, the identity of the host target genes which VGAM984 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36537] Nucleotide sequences of the VGAM984 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM984 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM984 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM984 are further described hereinbelow with reference to Table 1.

[36538] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM984 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM984 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36539] As mentioned hereinabove with reference to Fig. 1, a function of VGAM984 gene, herein designated VGAM is inhibition of expression of VGAM984 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM984 correlate with, and may be deduced from, the identity of the target genes which VGAM984 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36540] KIAA0442 (Accession NM_015570) is a VGAM984 host target gene. KIAA0442 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by KIAA0442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0442 BINDING SITE, designated SEQ ID:17842, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36541] A function of VGAM984 is therefore inhibition of KIAA0442 (Accession NM_015570). Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0442. KIAA0711 (Accession NM_014867) is another VGAM984 host target gene. KIAA0711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0711 BINDING SITE, designated SEQ ID:16953, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36542] Another function of VGAM984 is therefore inhibition of KIAA0711 (Accession NM_014867). Accordingly, utilities

of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0711. KIAA1240 (Accession XM_039676) is another VGAM984 host target gene. KIAA1240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1240 BINDING SITE, designated SEQ ID:33143, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36543] Another function of VGAM984 is therefore inhibition of KIAA1240 (Accession XM_039676). Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1240. PRO0245 (Accession NM_014122) is another VGAM984 host target gene. PRO0245 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0245

BINDING SITE, designated SEQ ID:15376, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36544] Another function of VGAM984 is therefore inhibition of PRO0245 (Accession NM_014122). Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0245. ZFD25 (Accession NM_016220) is another VGAM984 host target gene. ZFD25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFD25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFD25 BINDING SITE, designated SEQ ID:18319, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36545] Another function of VGAM984 is therefore inhibition of ZFD25 (Accession NM_016220). Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFD25. LOC157381 (Accession XM_098754) is another VGAM984 host target gene. LOC157381 BINDING SITE is HOST TAR-

GET binding site found in the 3' untranslated region of mRNA encoded by LOC157381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157381 BINDING SITE, designated SEQ ID:41792, to the nucleotide sequence of VGAM984 RNA, herein designated VGAM RNA, also designated SEQ ID:3695.

[36546] Another function of VGAM984 is therefore inhibition of LOC157381 (Accession XM_098754). Accordingly, utilities of VGAM984 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157381. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 985 (VGAM985) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36547] VGAM985 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM985 was detected is described hereinabove with reference to Figs. 1-8.

[36548] VGAM985 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36549] VGAM985 gene encodes a VGAM985 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM985 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM985 precursor RNA is designated SEQ ID:971, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:971 is located at position 26086 relative to the genome of Human Herpesvirus 3.

[36550] VGAM985 precursor RNA folds onto itself, forming VGAM985 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[36551] An enzyme complex designated DICER COMPLEX, `dices` the VGAM985 folded precursor RNA into VGAM985 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM985 RNA is designated SEQ ID:3696, and is provided hereinbelow with reference to the sequence listing part.

[36552] VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM985 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36553] VGAM985 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM985 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM985 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM985 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[36554] The complementary binding of VGAM985 RNA, herein designated VGAM RNA, to host target binding sites on VGAM985 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM985 host target RNA into VGAM985 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36555] It is appreciated that VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM985 host target genes. The mRNA of each one of this plurality of VGAM985 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM985 RNA, herein designated VGAM RNA, and which when bound by VGAM985 RNA causes inhibition of translation of respective one or more VGAM985 host target proteins.

[36556] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM985 gene, herein designated VGAM GENE, on one or more VGAM985 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36557] It is yet further appreciated that a function of VGAM985 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM985 correlate with, and may be deduced from, the identity of the host target genes which VGAM985 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36558] Nucleotide sequences of the VGAM985 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM985 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM985 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM985 are further described hereinbelow with reference to Table 1.

[36559] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM985 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM985 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36560] As mentioned hereinabove with reference to Fig. 1, a function of VGAM985 gene, herein designated VGAM is inhibition of expression of VGAM985 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM985 correlate with, and may be deduced from, the identity of the target genes which VGAM985 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36561] Myosin XVA (MYO15A, Accession NM_016239) is a VGAM985 host target gene. MYO15A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MYO15A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of MYO15A BINDING SITE, designated SEQ ID:18353, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36562] A function of VGAM985 is therefore inhibition of Myosin XVA (MYO15A, Accession NM_016239), a gene which acts as actin-based motors. Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO15A. The function of MYO15A has been established by previous studies. Shaker-2 (sh2) is a recessive mouse mutation on chromosome 11 that arose in the progeny of an x-ray irradiated mouse and has been proposed as the mouse model of DFNB3 (OMIM Ref. No. 600316), an autosomal recessive form of human deafness that maps to 17p11.2. Affected mice lack normal startle response to sound and show no auditory brain stem responses to sound pressure levels up to high levels, indicating profound deafness. Associated vestibular defects cause head-tossing and circling behavior. Fine genetic mapping of the sh2 gene identified 4 genes in a region of chromosome 11 that have homologs mapping to 17p11.2 in the human. Complete 1-Mb yeast artificial chromosome (YAC) and bacte-

rial artificial chromosome (BAC) contigs that spanned the shaker-2 critical region were generated. Because there were no compelling candidate genes in the nonrecombinant region, Probst et al. (1998) adopted an in vivo complementation approach to narrow the sh2 critical region. A BAC transgene from the shaker-2 critical region corrected the vestibular defects, deafness, and inner ear morphology of shaker-2 mice. An unconventional myosin gene, Myo15, was discovered by DNA sequencing of this BAC. Shaker-2 mice were found to have an amino acid substitution at a highly conserved position within the motor domain of this myosin. Auditory hair cells of shaker-2 mice have very short stereocilia and a long actin-containing protrusion extending from the basal end. This histopathology suggests that Myo15 is necessary for actin organization in the hair cells of the cochlea. In 3 consanguineous families from Pakistan and India, Liburd et al. (2001) found novel homozygous mutations in the MYO15A gene associated with profound congenital hearing loss, including Q1229X (602666.0004), IVS4+1G-T (602666.0005), and Q2716H (602666.0006). In addition, a hemizygous missense mutation, T2205I (602666.0007), was found in a patient with Smith-Magenis syndrome

(OMIM Ref. No. 182290) due to a deletion in 17p11.2. The patient had moderately severe hearing loss. The mother was heterozygous for the T2205I mutation.

[36563] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36564] Liburd, N.; Ghosh, M.; Riazuddin, S.; Naz, S.; Khan, S.; Ahmed, Z.; Riazuddin, S.; Liang, Y.; Menon, P. S. N.; Smith, T.; Smith, A. C. M.; Chen, K.-S.; Lupski, J. R.; Wilcox, E. R.; Potocki, L.; Friedman, T. B. : Novel mutations of MYO15A associated with profound deafness in consanguineous families and moderately severe hearing loss in a patient with Smith–Magenis syndrome. Hum. Genet. 109: 535–541, 2001. ; and

[36565] Probst, F. J.; Fridell, R. A.; Raphael, Y.; Saunders, T. L.; Wang, A.; Liang, Y.; Morell, R. J.; Touchman, J. W.; Lyons, R. H.; Noben–Trauth, K.; Friedman, T. B.; Camper, S. A. : Corre.

[36566] Further studies establishing the function and utilities of MYO15A are found in John Hopkins OMIM database record ID 602666, and in cited publications numbered 722 and 7223–7224 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence.KIAA0514 (Accession NM_014696) is another VGAM985 host target gene. KIAA0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16202, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36567] Another function of VGAM985 is therefore inhibition of KIAA0514 (Accession NM_014696). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. Mitogen-activated Protein Kinase Kinase 3 (MAP2K3, Accession NM_145109) is another VGAM985 host target gene. MAP2K3 BINDING SITE1 and MAP2K3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP2K3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K3 BINDING SITE1 and MAP2K3 BINDING SITE2,

designated SEQ ID:29713 and SEQ ID:8636 respectively, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36568] Another function of VGAM985 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 3 (MAP2K3, Accession NM_145109). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K3.

LOC148824 (Accession XM_097527) is another VGAM985 host target gene. LOC148824 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148824 BINDING SITE, designated SEQ ID:40906, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36569] Another function of VGAM985 is therefore inhibition of LOC148824 (Accession XM_097527). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148824. LOC219690 (Accession XM_167572) is an-

other VGAM985 host target gene. LOC219690 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC219690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219690 BINDING SITE, designated SEQ ID:44705, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36570] Another function of VGAM985 is therefore inhibition of LOC219690 (Accession XM_167572). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219690. LOC221431 (Accession XM_166380) is another VGAM985 host target gene. LOC221431 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221431 BINDING SITE, designated SEQ ID:44221, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36571] Another function of VGAM985 is therefore inhibition of LOC221431 (Accession XM_166380). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221431. LOC255533 (Accession XM_173073) is another VGAM985 host target gene. LOC255533 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255533 BINDING SITE, designated SEQ ID:46329, to the nucleotide sequence of VGAM985 RNA, herein designated VGAM RNA, also designated SEQ ID:3696.

[36572] Another function of VGAM985 is therefore inhibition of LOC255533 (Accession XM_173073). Accordingly, utilities of VGAM985 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255533. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 986 (VGAM986) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[36573] VGAM986 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM986 was detected is described hereinabove with reference to Figs. 1–8.

[36574] VGAM986 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–4. VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36575] VGAM986 gene encodes a VGAM986 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM986 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM986 precursor RNA is designated SEQ ID:972, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:972 is located at position 377 relative to the genome of Leishmania RNA Virus 1–4.

[36576] VGAM986 precursor RNA folds onto itself, forming VGAM986 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36577] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM986 folded precursor RNA into VGAM986 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 43%) nucleotide se-
quence of VGAM986 RNA is designated SEQ ID:3697, and
is provided hereinbelow with reference to the sequence
listing part.

[36578] VGAM986 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM986 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM986 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36579] VGAM986 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM986 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM986 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36580] The complementary binding of VGAM986 RNA, herein designated VGAM RNA, to host target binding sites on VGAM986 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM986 host target RNA into VGAM986 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36581] It is appreciated that VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM986 host target genes. The mRNA of each one of this plurality of VGAM986 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM986 RNA, herein designated VGAM RNA, and which when bound by VGAM986 RNA causes inhibition of translation of respective one or more VGAM986 host target proteins.

[36582] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM986 gene, herein designated VGAM GENE, on one or more VGAM986 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36583] It is yet further appreciated that a function of VGAM986 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-4. Specific functions, and accordingly utilities, of VGAM986 correlate with, and may be deduced from, the identity of the host target genes which VGAM986 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [36584] Nucleotide sequences of the VGAM986 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM986 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM986 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM986 are further described hereinbelow with reference to Table 1.
- [36585] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM986 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM986 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36586] As mentioned hereinabove with reference to Fig. 1, a function of VGAM986 gene, herein designated VGAM is inhibition of expression of VGAM986 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM986 correlate with, and may be deduced from, the identity of the target genes which VGAM986 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36587] SudD Suppressor of BimD6 Homolog (*A. nidulans*) (SUDD, Accession NM_003831) is a VGAM986 host target gene. SUDD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUDD BINDING SITE, designated SEQ ID:9922, to the nucleotide sequence of VGAM986 RNA, herein designated VGAM RNA, also designated SEQ ID:3697.

[36588] A function of VGAM986 is therefore inhibition of SudD Suppressor of BimD6 Homolog (*A. nidulans*) (SUDD, Accession NM_003831). Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUDD. Von Hippel-Lindau Binding Protein 1 (VBP1, Accession NM_003372) is another VGAM986 host target gene. VBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VBP1 BINDING SITE, designated SEQ ID:9399, to the nucleotide sequence

of VGAM986 RNA, herein designated VGAM RNA, also designated SEQ ID:3697.

[36589] Another function of VGAM986 is therefore inhibition of Von Hippel–Lindau Binding Protein 1 (VBP1, Accession NM_003372), a gene which binds specifically to cytosolic chaperonin (c-cpn) and transfers target proteins to it. Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VBP1. The function of VBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM945. Vasoactive Intestinal Peptide (VIP, Accession NM_003381) is another VGAM986 host target gene. VIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIP BINDING SITE, designated SEQ ID:9411, to the nucleotide sequence of VGAM986 RNA, herein designated VGAM RNA, also designated SEQ ID:3697.

[36590] Another function of VGAM986 is therefore inhibition of

Vasoactive Intestinal Peptide (VIP, Accession NM_003381), a gene which causes vasodilation, lowers arterial blood pressure, stimulates myocardial contractility, increases glycogenolysis and relaxes the smooth muscle . Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIP. The function of VIP has been established by previous studies. Vasoactive intestinal peptide is a neuropeptide present in the lymphoid microenvironment that elicits a broad spectrum of biologic functions, including the modulation of innate and adaptive immunity, and shows a predominant antiinflammatory action. VIP promotes TH2 differentiation and inhibits TH1 responses by regulating macrophage costimulatory signals and probably IL12/IFN-gamma production. In collagen-induced arthritis, a murine model for rheumatoid arthritis, Delgado et al. (2001) administered VIP daily or on alternate days for 2 weeks. Treatment with VIP significantly reduced incidence and severity of arthritis in this model, completely abrogating joint swelling and destruction of cartilage and bone. The therapeutic effect of VIP was associated with downregulation of both inflammatory and autoimmune components of the disease. Delgado et al. (2001) con-

cluded that VIP is a viable candidate for the development of treatments for rheumatoid arthritis. Vasoactive intestinal peptide is a neuropeptide present in the lymphoid microenvironment that elicits a broad spectrum of biologic functions, including the modulation of innate and adaptive immunity, and shows a predominant antiinflammatory action. VIP promotes TH2 differentiation and inhibits TH1 responses by regulating macrophage costimulatory signals and probably IL12/IFN-gamma production. In collagen-induced arthritis, a murine model for rheumatoid arthritis, Delgado et al. (2001) administered VIP daily or on alternate days for 2 weeks. Treatment with VIP significantly reduced incidence and severity of arthritis in this model, completely abrogating joint swelling and destruction of cartilage and bone. The therapeutic effect of VIP was associated with downregulation of both inflammatory and autoimmune components of the disease. Delgado et al. (2001) concluded that VIP is a viable candidate for the development of treatments for rheumatoid arthritis.

[36591] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36592] Linder, S.; Barkhem, T.; Norberg, A.; Persson, H.;

Schalling, M.; Hokfelt, T.; Magnusson, G. : Structure and expression of the gene encoding the vasoactive intestinal peptide precursor. Proc. Nat. Acad. Sci. 84: 605–609, 1987. ; and

[36593] Delgado, M.; Abad, C.; Martinez, C.; Leceta, J.; Gomariz, R. P. : Vasoactive intestinal peptide prevents experimental arthritis by downregulating both autoimmune and inflammatory component.

[36594] Further studies establishing the function and utilities of VIP are found in John Hopkins OMIM database record ID 192320, and in cited publications numbered 9663–967 and 11146 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC144467 (Accession NM_138473) is another VGAM986 host target gene. LOC144467 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144467 BINDING SITE, designated SEQ ID:28820, to the nucleotide sequence of VGAM986 RNA, herein designated VGAM RNA, also designated SEQ ID:3697.

[36595] Another function of VGAM986 is therefore inhibition of LOC144467 (Accession NM_138473). Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144467. LOC50999 (Accession NM_016040) is another VGAM986 host target gene. LOC50999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC50999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC50999 BINDING SITE, designated SEQ ID:18115, to the nucleotide sequence of VGAM986 RNA, herein designated VGAM RNA, also designated SEQ ID:3697.

[36596] Another function of VGAM986 is therefore inhibition of LOC50999 (Accession NM_016040). Accordingly, utilities of VGAM986 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC50999. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 987 (VGAM987) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[36597] VGAM987 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM987 was detected is described hereinabove with reference to Figs. 1–8.

[36598] VGAM987 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–4. VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36599] VGAM987 gene encodes a VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM987 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM987 precursor RNA is designated SEQ ID:973, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:973 is located at position 1955 relative to the genome of Leishmania RNA Virus 1–4.

[36600] VGAM987 precursor RNA folds onto itself, forming VGAM987 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36601] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM987 folded precursor RNA into VGAM987 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 52%) nucleotide se-
quence of VGAM987 RNA is designated SEQ ID:3698, and
is provided hereinbelow with reference to the sequence
listing part.

[36602] VGAM987 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM987 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM987 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36603] VGAM987 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM987 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM987 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36604] The complementary binding of VGAM987 RNA, herein designated VGAM RNA, to host target binding sites on VGAM987 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM987 host target RNA into VGAM987 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36605] It is appreciated that VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM987 host target genes. The mRNA of each one of this plurality of VGAM987 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM987 RNA, herein designated VGAM RNA, and which when bound by VGAM987 RNA causes inhibition of translation of respective one or more VGAM987 host target proteins.

[36606] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM987 gene, herein designated VGAM GENE, on one or more VGAM987 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36607] It is yet further appreciated that a function of VGAM987 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-4. Specific functions, and accordingly utilities, of VGAM987 correlate with, and may be deduced from, the identity of the host target genes which VGAM987 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[36608] Nucleotide sequences of the VGAM987 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM987 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM987 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM987 are further described hereinbelow with reference to Table 1.

[36609] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM987 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM987 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36610] As mentioned hereinabove with reference to Fig. 1, a function of VGAM987 gene, herein designated VGAM is inhibition of expression of VGAM987 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM987 correlate with, and may be deduced from, the identity of the target genes which VGAM987 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36611] MGC2835 (Accession NM_024072) is a VGAM987 host target gene. MGC2835 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC2835, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2835 BINDING SITE, designated SEQ ID:23503, to the nucleotide sequence of VGAM987 RNA, herein designated VGAM RNA, also designated SEQ ID:3698.

[36612] A function of VGAM987 is therefore inhibition of MGC2835 (Accession NM_024072). Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2835. LOC143888 (Accession XM_084669) is another VGAM987 host target gene. LOC143888 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143888 BINDING SITE, designated SEQ ID:37667, to the nucleotide sequence of VGAM987 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3698.

[36613] Another function of VGAM987 is therefore inhibition of LOC143888 (Accession XM_084669). Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143888. LOC148709 (Accession XM_086281) is another VGAM987 host target gene. LOC148709 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148709 BINDING SITE, designated SEQ ID:38582, to the nucleotide sequence of VGAM987 RNA, herein designated VGAM RNA, also designated SEQ ID:3698.

[36614] Another function of VGAM987 is therefore inhibition of LOC148709 (Accession XM_086281). Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148709. LOC257017 (Accession XM_173227) is another VGAM987 host target gene. LOC257017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257017, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257017 BINDING SITE, designated SEQ ID:46492, to the nucleotide sequence of VGAM987 RNA, herein designated VGAM RNA, also designated SEQ ID:3698.

[36615] Another function of VGAM987 is therefore inhibition of LOC257017 (Accession XM_173227). Accordingly, utilities of VGAM987 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257017. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 988 (VGAM988) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36616] VGAM988 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM988 was detected is described hereinabove with reference to Figs. 1–8.

[36617] VGAM988 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus

1-4. VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36618] VGAM988 gene encodes a VGAM988 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM988 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM988 precursor RNA is designated SEQ ID:974, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:974 is located at position 2513 relative to the genome of Leishmania RNA Virus 1-4.

[36619] VGAM988 precursor RNA folds onto itself, forming VGAM988 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36620] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM988 folded precursor RNA into VGAM988 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM988 RNA is designated SEQ ID:3699, and is provided hereinbelow with reference to the sequence listing part.

[36621] VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM988 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36622] VGAM988 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM988 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM988 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36623] The complementary binding of VGAM988 RNA, herein designated VGAM RNA, to host target binding sites on VGAM988 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM988 host target RNA into VGAM988 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36624] It is appreciated that VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM988 host target genes. The mRNA of each one of this plurality of VGAM988 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM988 RNA, herein designated VGAM RNA, and which when bound by VGAM988 RNA causes inhibition of translation of respective one or more VGAM988 host target proteins.

[36625] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM988 gene, herein designated VGAM GENE, on one or more VGAM988 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36626] It is yet further appreciated that a function of VGAM988 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-4. Specific functions, and accordingly utilities, of VGAM988 correlate with, and may be deduced from, the identity of the host target genes which VGAM988 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36627] Nucleotide sequences of the VGAM988 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM988 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM988 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM988 are further described hereinbelow with reference to Table 1.

[36628] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM988 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM988 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36629] As mentioned hereinabove with reference to Fig. 1, a function of VGAM988 gene, herein designated VGAM is inhibition of expression of VGAM988 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM988 correlate with, and may be deduced from, the identity of the target genes which VGAM988 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36630] BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519) is a VGAM988 host target gene. BRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRF1

BINDING SITE, designated SEQ ID:7259, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36631] A function of VGAM988 is therefore inhibition of BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519), a gene which is a general activator of RNA polymerase III. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRF1. The function of BRF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Ladinin 1 (LAD1, Accession NM_005558) is another VGAM988 host target gene. LAD1 BINDING SITE1 and LAD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LAD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAD1 BINDING SITE1 and LAD1 BINDING SITE2, designated SEQ ID:12088 and SEQ ID:12087 respectively, to the nucleotide sequence of VGAM988 RNA, herein designated

VGAM RNA, also designated SEQ ID:3699.

[36632] Another function of VGAM988 is therefore inhibition of Ladinin 1 (LAD1, Accession NM_005558). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAD1. RAB7, Member RAS Oncogene Family (RAB7, Accession NM_004637) is another VGAM988 host target gene. RAB7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB7 BINDING SITE, designated SEQ ID:11012, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36633] Another function of VGAM988 is therefore inhibition of RAB7, Member RAS Oncogene Family (RAB7, Accession NM_004637), a gene which is an important regulator of vesicular transport in the late endocytic pathway. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB7. The function of RAB7 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM35. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 2 (RPS6KA2, Accession NM_021135) is another VGAM988 host target gene. RPS6KA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RPS6KA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA2 BINDING SITE, designated SEQ ID:22107, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36634] Another function of VGAM988 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 2 (RPS6KA2, Accession NM_021135), a gene which phosphorylates a wide range of substrates including ribosomal protein s6. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA2. The function of RPS6KA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM216. Secreted Frizzled-related Protein 1 (SFRP1, Ac-

cession NM_003012) is another VGAM988 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BINDING SITE, designated SEQ ID:8930, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36635] Another function of VGAM988 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250. VENT-like Homeobox 2 (VENTX2, Accession NM_014468) is another VGAM988 host target gene. VENTX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

VENTX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VENTX2 BINDING SITE, designated SEQ ID:15818, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36636] Another function of VGAM988 is therefore inhibition of VENT-like Homeobox 2 (VENTX2, Accession NM_014468). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VENTX2. DKFZP564O0423 (Accession XM_166254) is another VGAM988 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44072, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36637] Another function of VGAM988 is therefore inhibition of

DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. FK506 Binding Protein 4, 59kDa (FKBP4, Accession NM_002014) is another VGAM988 host target gene. FKBP4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FKBP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP4 BINDING SITE, designated SEQ ID:7755, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36638] Another function of VGAM988 is therefore inhibition of FK506 Binding Protein 4, 59kDa (FKBP4, Accession NM_002014). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP4. FLJ10932 (Accession NM_018277) is another VGAM988 host target gene. FLJ10932 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10932, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10932 BINDING SITE, designated SEQ ID:20266, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36639] Another function of VGAM988 is therefore inhibition of FLJ10932 (Accession NM_018277). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10932. FLJ13397 (Accession NM_024948) is another VGAM988 host target gene. FLJ13397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13397 BINDING SITE, designated SEQ ID:24501, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36640] Another function of VGAM988 is therefore inhibition of FLJ13397 (Accession NM_024948). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ13397. FLJ22393 (Accession NM_025106) is another VGAM988 host target gene. FLJ22393 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22393, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22393 BINDING SITE, designated SEQ ID:24757, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36641] Another function of VGAM988 is therefore inhibition of FLJ22393 (Accession NM_025106). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22393. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130) is another VGAM988 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GOLPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLPH3 BINDING SITE, designated SEQ

ID:22687, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36642] Another function of VGAM988 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLPH3. MGC15482 (Accession NM_032875) is another VGAM988 host target gene. MGC15482 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15482 BINDING SITE, designated SEQ ID:26697, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36643] Another function of VGAM988 is therefore inhibition of MGC15482 (Accession NM_032875). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15482. Ornithine Decarboxylase Antizyme Inhibitor

(OAZIN, Accession NM_015878) is another VGAM988 host target gene. OAZIN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by OAZIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAZIN BINDING SITE, designated SEQ ID:18021, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36644] Another function of VGAM988 is therefore inhibition of Ornithine Decarboxylase Antizyme Inhibitor (OAZIN, Accession NM_015878). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAZIN. Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM_021003) is another VGAM988 host target gene. PPM1A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PPM1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPM1A BINDING SITE,

designated SEQ ID:21999, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36645] Another function of VGAM988 is therefore inhibition of Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM_021003). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPM1A. Rab11-FIP2 (Accession NM_014904) is another VGAM988 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17099, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36646] Another function of VGAM988 is therefore inhibition of Rab11-FIP2 (Accession NM_014904). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11-FIP2. RCD-8 (Accession NM_014329) is another

VGAM988 host target gene. RCD-8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RCD-8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RCD-8 BINDING SITE, designated SEQ ID:15643, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36647] Another function of VGAM988 is therefore inhibition of RCD-8 (Accession NM_014329). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RCD-8. REC8 (Accession NM_005132) is another VGAM988 host target gene. REC8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by REC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REC8 BINDING SITE, designated SEQ ID:11609, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36648] Another function of VGAM988 is therefore inhibition of REC8 (Accession NM_005132). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REC8. TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM_021809) is another VGAM988 host target gene. TGIF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGIF2 BINDING SITE, designated SEQ ID:22367, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36649] Another function of VGAM988 is therefore inhibition of TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM_021809). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGIF2. Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285) is another VGAM988 host target gene. TP53INP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

TP53INP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53INP1 BINDING SITE, designated SEQ ID:27108, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36650] Another function of VGAM988 is therefore inhibition of Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53INP1.

LOC139411 (Accession XM_066680) is another VGAM988 host target gene. LOC139411 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139411 BINDING SITE, designated SEQ ID:37342, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36651] Another function of VGAM988 is therefore inhibition of

LOC139411 (Accession XM_066680). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139411. LOC146433 (Accession XM_085458) is another VGAM988 host target gene. LOC146433 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146433, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146433 BINDING SITE, designated SEQ ID:38147, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36652] Another function of VGAM988 is therefore inhibition of LOC146433 (Accession XM_085458). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146433. LOC51104 (Accession NM_016014) is another VGAM988 host target gene. LOC51104 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC51104 BINDING SITE, designated SEQ ID:18091, to the nucleotide sequence of VGAM988 RNA, herein designated VGAM RNA, also designated SEQ ID:3699.

[36653] Another function of VGAM988 is therefore inhibition of LOC51104 (Accession NM_016014). Accordingly, utilities of VGAM988 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51104. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 989 (VGAM989) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36654] VGAM989 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM989 was detected is described hereinabove with reference to Figs. 1–8.

[36655] VGAM989 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–4. VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[36656] VGAM989 gene encodes a VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM989 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM989 precursor RNA is designated SEQ ID:975, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:975 is located at position 1535 relative to the genome of Leishmania RNA Virus 1-4.

[36657] VGAM989 precursor RNA folds onto itself, forming VGAM989 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36658] An enzyme complex designated DICER COMPLEX, `dices` the VGAM989 folded precursor RNA into VGAM989 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM989 RNA is designated SEQ ID:3700, and is provided hereinbelow with reference to the sequence listing part.

[36659] VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM989 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36660] VGAM989 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM989 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM989 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36661] The complementary binding of VGAM989 RNA, herein designated VGAM RNA, to host target binding sites on VGAM989 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM989 host target RNA into VGAM989 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36662] It is appreciated that VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM989 host target genes. The mRNA of each one of this plurality of VGAM989 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM989 RNA, herein designated VGAM RNA, and which when bound by VGAM989 RNA causes inhibition of translation of respective one or more VGAM989 host target proteins.

[36663] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM989 gene, herein designated VGAM GENE, on one or more VGAM989 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36664] It is yet further appreciated that a function of VGAM989 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM989 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-4. Specific functions, and accordingly utilities, of VGAM989 correlate with, and may be deduced from, the identity of the host target genes which VGAM989 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36665] Nucleotide sequences of the VGAM989 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM989 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM989 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM989 are further described hereinbelow with reference to Table 1.

[36666] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM989 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM989 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36667] As mentioned hereinabove with reference to Fig. 1, a function of VGAM989 gene, herein designated VGAM is inhibition of expression of VGAM989 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM989 correlate with, and may be deduced from, the identity of the target genes which VGAM989 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36668] Chromosome 7 Open Reading Frame 2 (C7orf2, Accession NM_022458) is a VGAM989 host target gene. C7orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C7orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7orf2 BINDING SITE, designated SEQ ID:22795, to the nucleotide sequence of VGAM989 RNA, herein designated VGAM RNA, also designated SEQ ID:3700.

[36669] A function of VGAM989 is therefore inhibition of Chromosome 7 Open Reading Frame 2 (C7orf2, Accession NM_022458). Accordingly, utilities of VGAM989 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7orf2. FLJ14054 (Accession NM_024563) is another VGAM989 host target gene. FLJ14054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14054 BINDING SITE, designated SEQ ID:23783, to the nucleotide sequence of VGAM989 RNA, herein designated VGAM RNA, also designated SEQ ID:3700.

[36670] Another function of VGAM989 is therefore inhibition of FLJ14054 (Accession NM_024563). Accordingly, utilities of VGAM989 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14054. FLJ20297 (Accession NM_017751) is another VGAM989 host target gene. FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20297, cor-

responding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2, designated SEQ ID:19358 and SEQ ID:19648 respectively, to the nucleotide sequence of VGAM989 RNA, herein designated VGAM RNA, also designated SEQ ID:3700.

[36671] Another function of VGAM989 is therefore inhibition of FLJ20297 (Accession NM_017751). Accordingly, utilities of VGAM989 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20297. LOC150776 (Accession XM_032542) is another VGAM989 host target gene. LOC150776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150776 BINDING SITE, designated SEQ ID:31675, to the nucleotide sequence of VGAM989 RNA, herein designated VGAM RNA, also designated SEQ ID:3700.

[36672] Another function of VGAM989 is therefore inhibition of LOC150776 (Accession XM_032542). Accordingly, utilities

of VGAM989 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150776. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 990 (VGAM990) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36673] VGAM990 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM990 was detected is described hereinabove with reference to Figs. 1–8.

[36674] VGAM990 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–4. VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36675] VGAM990 gene encodes a VGAM990 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM990 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM990 precursor RNA is designated SEQ ID:976, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:976 is located at position 5193 relative to the genome of Leishmania RNA Virus 1-4.

[36676] VGAM990 precursor RNA folds onto itself, forming VGAM990 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36677] An enzyme complex designated DICER COMPLEX, `dices` the VGAM990 folded precursor RNA into VGAM990 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM990 RNA is designated SEQ ID:3701, and

is provided hereinbelow with reference to the sequence listing part.

[36678] VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM990 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36679] VGAM990 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM990 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM990 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36680] The complementary binding of VGAM990 RNA, herein designated VGAM RNA, to host target binding sites on VGAM990 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM990 host target RNA into VGAM990 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36681] It is appreciated that VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM990 host target genes. The mRNA of each one of this plurality of VGAM990 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM990 RNA, herein designated VGAM RNA, and which when bound by VGAM990 RNA causes inhibition of translation of respective one or more VGAM990 host target proteins.

[36682] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM990 gene, herein designated VGAM GENE, on one or more VGAM990 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36683] It is yet further appreciated that a function of VGAM990 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1–4. Specific functions, and accordingly utilities, of VGAM990 correlate with, and may be deduced from, the identity of the host target genes which VGAM990 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36684] Nucleotide sequences of the VGAM990 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM990 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM990 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM990 are further described hereinbelow with reference to Table 1.

[36685] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM990 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM990 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36686] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM990 gene, herein designated VGAM is inhibition of expression of VGAM990 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM990 correlate with, and may be deduced from, the identity of the target genes which VGAM990 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36687] Down Syndrome Critical Region Gene 1 (DSCR1, Accession NM_004414) is a VGAM990 host target gene. DSCR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR1 BINDING SITE, designated SEQ ID:10676, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36688] A function of VGAM990 is therefore inhibition of Down Syndrome Critical Region Gene 1 (DSCR1, Accession NM_004414), a gene which inhibits calcineurin-dependent transcriptional responses. Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR1.

The function of DSCR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM589. Epithelial Membrane Protein 1 (EMP1, Accession NM_001423) is another VGAM990 host target gene. EMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMP1 BINDING SITE, designated SEQ ID:7136, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36689] Another function of VGAM990 is therefore inhibition of Epithelial Membrane Protein 1 (EMP1, Accession NM_001423), a gene which plays a role in squamous cell differentiation; member of the PMP22/EMP/MP20 family of membrane glycoproteins. Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMP1. The function of EMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM107.Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM990 host target gene. SEDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEDL BINDING SITE, designated SEQ ID:15914, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36690] Another function of VGAM990 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.Zinc Finger Protein 22 (KOX 15) (ZNF22, Accession XM_166153) is another VGAM990 host target gene. ZNF22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by ZNF22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF22 BINDING SITE, designated SEQ ID:43970, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36691] Another function of VGAM990 is therefore inhibition of Zinc Finger Protein 22 (KOX 15) (ZNF22, Accession XM_166153). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF22. ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726) is another VGAM990 host target gene. ABCC13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC13 BINDING SITE, designated SEQ ID:28972, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36692] Another function of VGAM990 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC13. FLJ20308 (Accession XM_039852) is another VGAM990 host target gene. FLJ20308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20308 BINDING SITE, designated SEQ ID:33199, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36693] Another function of VGAM990 is therefore inhibition of FLJ20308 (Accession XM_039852). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20308. KIAA1511 (Accession XM_046581) is another VGAM990 host target gene. KIAA1511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1511, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1511 BINDING SITE, designated SEQ ID:34756, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36694] Another function of VGAM990 is therefore inhibition of KIAA1511 (Accession XM_046581). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1511. MGC23980 (Accession NM_145005) is another VGAM990 host target gene. MGC23980 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC23980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC23980 BINDING SITE, designated SEQ ID:29606, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36695] Another function of VGAM990 is therefore inhibition of MGC23980 (Accession NM_145005). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC23980. WSB1 (Accession NM_134264) is another VGAM990 host target gene. WSB1 BINDING SITE1 and WSB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WSB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WSB1 BINDING SITE1 and WSB1 BINDING SITE2, designated SEQ ID:28616 and SEQ ID:28622 respectively, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36696] Another function of VGAM990 is therefore inhibition of WSB1 (Accession NM_134264). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WSB1. LOC154043 (Accession XM_087831) is another VGAM990 host target gene. LOC154043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154043 BINDING

SITE, designated SEQ ID:39460, to the nucleotide sequence of VGAM990 RNA, herein designated VGAM RNA, also designated SEQ ID:3701.

[36697] Another function of VGAM990 is therefore inhibition of LOC154043 (Accession XM_087831). Accordingly, utilities of VGAM990 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154043. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 991 (VGAM991) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36698] VGAM991 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM991 was detected is described hereinabove with reference to Figs. 1–8.

[36699] VGAM991 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36700] VGAM991 gene encodes a VGAM991 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM991 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM991 precursor RNA is designated SEQ ID:977, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:977 is located at position 390 relative to the genome of Leishmania RNA Virus 1-1.

[36701] VGAM991 precursor RNA folds onto itself, forming VGAM991 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36702] An enzyme complex designated DICER COMPLEX, `dices` the VGAM991 folded precursor RNA into VGAM991 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM991 RNA is designated SEQ ID:3702, and is provided hereinbelow with reference to the sequence listing part.

[36703] VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM991 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36704] VGAM991 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM991 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM991 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[36705] The complementary binding of VGAM991 RNA, herein designated VGAM RNA, to host target binding sites on VGAM991 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM991 host target RNA into VGAM991 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36706] It is appreciated that VGAM991 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM991 host target genes. The mRNA of each one of this plurality of VGAM991 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM991 RNA, herein designated VGAM RNA, and which when bound by VGAM991 RNA causes inhibition of translation of respective one or more VGAM991 host target proteins.

[36707] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM991 gene, herein designated VGAM GENE, on one or more VGAM991 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[36708] It is yet further appreciated that a function of VGAM991 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM991 correlate with, and may be deduced from, the identity of the host target genes which VGAM991 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36709] Nucleotide sequences of the VGAM991 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM991 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM991 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM991 are further described hereinbelow with reference to Table 1.

[36710] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM991 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM991 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36711] As mentioned hereinabove with reference to Fig. 1, a function of VGAM991 gene, herein designated VGAM is inhibition of expression of VGAM991 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM991 correlate with, and may be deduced from, the identity of the target genes which VGAM991 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36712] Anterior Gradient 2 Homolog (*Xenopus laevis*) (AGR2, Accession NM_006408) is a VGAM991 host target gene. AGR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AGR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGR2 BINDING SITE, designated SEQ ID:13113, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36713] A function of VGAM991 is therefore inhibition of Anterior

Gradient 2 Homolog (*Xenopus laevis*) (AGR2, Accession NM_006408), a gene which Expressed in estrogen receptor-positive breast cancer cell lines. Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGR2. The function of AGR2 has been established by previous studies. Estrogen receptor (ER; 133430)-negative breast cancers are less well-differentiated and more aggressive than ER-positive tumors. Using suppression subtractive hybridization, Kuang et al. (1998) identified 29 gene fragments expressed in ER-positive breast carcinomas that might contribute to its less aggressive phenotype compared to ER-negative tumors. The expression of one of these fragments, DEME2, correlated with ER expression in 8 breast carcinoma cell lines. By screening an ER-positive breast cancer cDNA library with the DEKE2 fragment, followed by EST database searching, Thompson and Weigel (1998) obtained a cDNA encoding AGR2, a homolog of the frog secreted cement gland anterior gradient protein, which they termed AG2. The deduced 175-amino acid soluble AGR2 protein, which is 91% identical to the mouse protein and 47% identical to the frog protein, contains a signal peptide. Northern blot analysis revealed strongest

expression of 0.9– and 1.6–kb AGR2 transcripts in lung and in all ER–positive breast carcinoma lines tested; weaker expression was detected in pancreas. RNA dot blot analysis detected strong expression in trachea, lung, stomach, colon, prostate, and small intestine, with lower expression in other tissues. By radiation hybrid analysis and FISH, Petek et al. (2000) mapped the AGR2 gene to 7p21.3.

[36714] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36715] Petek, E.; Windpassinger, C.; Egger, H.; Kroisel, P. M.; Wagner, K. : Localization of the human anterior gradient–2 gene (AGR2) to chromosome band 7p21.3 by radiation hybrid mapping and fluorescence in situ hybridisation. *Cytogenet. Cell Genet.* 89: 141–142, 2000. ; and

[36716] Thompson, D. A.; Weigel, R. J. : hAG–2, the human homologue of the *Xenopus laevis* cement gland gene XAG–2, is coexpressed with estrogen receptor in breast cancer cell lines. *Biochem. B.*

[36717] Further studies establishing the function and utilities of AGR2 are found in John Hopkins OMIM database record ID 606358, and in cited publications numbered 6420–6173

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598) is another VGAM991 host target gene. SLC12A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC12A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A7 BINDING SITE, designated SEQ ID:13374, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36718] Another function of VGAM991 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598), a gene which is a potassium/chloride-cotransporter. Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A7. The function of SLC12A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.CLIPR-59

(Accession NM_015526) is another VGAM991 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59 BINDING SITE, designated SEQ ID:17784, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36719] Another function of VGAM991 is therefore inhibition of CLIPR-59 (Accession NM_015526). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. DCNP1 (Accession NM_130848) is another VGAM991 host target gene. DCNP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DCNP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCNP1 BINDING SITE, designated SEQ ID:28386, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ

ID:3702.

[36720] Another function of VGAM991 is therefore inhibition of DCNP1 (Accession NM_130848). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCNP1. FLJ12875 (Accession NM_024544) is another VGAM991 host target gene. FLJ12875 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12875, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12875 BINDING SITE, designated SEQ ID:23753, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36721] Another function of VGAM991 is therefore inhibition of FLJ12875 (Accession NM_024544). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12875. KIAA0323 (Accession XM_032634) is another VGAM991 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31686, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36722] Another function of VGAM991 is therefore inhibition of KIAA0323 (Accession XM_032634). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. LOC144308 (Accession XM_096575) is another VGAM991 host target gene. LOC144308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144308 BINDING SITE, designated SEQ ID:40404, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36723] Another function of VGAM991 is therefore inhibition of LOC144308 (Accession XM_096575). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC144308. LOC153480 (Accession XM_053483) is another VGAM991 host target gene. LOC153480 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC153480, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153480 BINDING SITE, designated SEQ ID:36088, to the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36724] Another function of VGAM991 is therefore inhibition of LOC153480 (Accession XM_053483). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153480. LOC154739 (Accession XM_098602) is another VGAM991 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41722, to

the nucleotide sequence of VGAM991 RNA, herein designated VGAM RNA, also designated SEQ ID:3702.

[36725] Another function of VGAM991 is therefore inhibition of LOC154739 (Accession XM_098602). Accordingly, utilities of VGAM991 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 992 (VGAM992) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36726] VGAM992 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM992 was detected is described hereinabove with reference to Figs. 1–8.

[36727] VGAM992 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36728] VGAM992 gene encodes a VGAM992 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM992 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM992 precursor RNA is designated SEQ ID:978, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:978 is located at position 3813 relative to the genome of Leishmania RNA Virus 1-1.

[36729] VGAM992 precursor RNA folds onto itself, forming VGAM992 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36730] An enzyme complex designated DICER COMPLEX, `dices` the VGAM992 folded precursor RNA into VGAM992 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM992 RNA is designated SEQ ID:3703, and is provided hereinbelow with reference to the sequence listing part.

[36731] VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM992 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36732] VGAM992 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM992 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM992 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36733] The complementary binding of VGAM992 RNA, herein designated VGAM RNA, to host target binding sites on VGAM992 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM992 host target RNA into VGAM992 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36734] It is appreciated that VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM992 host target genes. The mRNA of each one of this plurality of VGAM992 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM992 RNA, herein designated VGAM RNA, and which when bound by VGAM992 RNA causes inhibition of translation of respective one or more VGAM992 host target proteins.

[36735] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM992 gene, herein designated VGAM GENE, on one or more VGAM992 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[36736] It is yet further appreciated that a function of VGAM992 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM992 correlate with, and may be deduced from, the identity of the host target genes which VGAM992 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36737] Nucleotide sequences of the VGAM992 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM992 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM992 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM992 are further described hereinbelow with reference to Table 1.

[36738] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM992 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM992 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36739] As mentioned hereinabove with reference to Fig. 1, a function of VGAM992 gene, herein designated VGAM is inhibition of expression of VGAM992 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM992 correlate with, and may be deduced from, the identity of the target genes which VGAM992 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36740] EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838) is a VGAM992 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41879, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36741] A function of VGAM992 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838).

Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Leucine-rich Repeat-containing 2 (LRRC2, Accession NM_024512) is another VGAM992 host target gene. LRRC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRRC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRC2 BINDING SITE, designated SEQ ID:23703, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36742] Another function of VGAM992 is therefore inhibition of Leucine-rich Repeat-containing 2 (LRRC2, Accession NM_024512). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRC2. Zinc Finger Protein, Subfamily 2A (FYVE domain containing), 1 (ZNFN2A1, Accession XM_027302) is another VGAM992 host target gene. ZNFN2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNFN2A1, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNFN2A1 BINDING SITE, designated SEQ ID:30468, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36743] Another function of VGAM992 is therefore inhibition of Zinc Finger Protein, Subfamily 2A (FYVE domain containing), 1 (ZNFN2A1, Accession XM_027302). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNFN2A1. Calsenilin, Presenilin Binding Protein, EF Hand Transcription Factor (CSEN, Accession NM_013434) is another VGAM992 host target gene. CSEN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSEN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSEN BINDING SITE, designated SEQ ID:15091, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36744] Another function of VGAM992 is therefore inhibition of

Calsenilin, Presenilin Binding Protein, EF Hand Transcription Factor (CSEN, Accession NM_013434). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSEN. Docking Protein 4 (DOK4, Accession NM_018110) is another VGAM992 host target gene. DOK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOK4 BINDING SITE, designated SEQ ID:19879, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36745] Another function of VGAM992 is therefore inhibition of Docking Protein 4 (DOK4, Accession NM_018110). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOK4. FLJ11800 (Accession NM_024974) is another VGAM992 host target gene. FLJ11800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11800, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11800 BINDING SITE, designated SEQ ID:24531, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36746] Another function of VGAM992 is therefore inhibition of FLJ11800 (Accession NM_024974). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11800. FLJ22341 (Accession NM_024599) is another VGAM992 host target gene. FLJ22341 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22341 BINDING SITE, designated SEQ ID:23847, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36747] Another function of VGAM992 is therefore inhibition of FLJ22341 (Accession NM_024599). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22341.

KIAA1950 (Accession XM_166532) is another VGAM992 host target gene. KIAA1950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1950 BINDING SITE, designated SEQ ID:44487, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36748] Another function of VGAM992 is therefore inhibition of KIAA1950 (Accession XM_166532). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1950. MGC15631 (Accession NM_032753) is another VGAM992 host target gene. MGC15631 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15631, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15631 BINDING SITE, designated SEQ ID:26494, to the nucleotide sequence of VGAM992 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3703.

[36749] Another function of VGAM992 is therefore inhibition of MGC15631 (Accession NM_032753). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15631. PRO2133 (Accession NM_018619) is another VGAM992 host target gene. PRO2133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2133 BINDING SITE, designated SEQ ID:20693, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36750] Another function of VGAM992 is therefore inhibition of PRO2133 (Accession NM_018619). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2133. Sialyltransferase 4A (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM_003033) is another VGAM992 host target gene. SIAT4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SIAT4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT4A BINDING SITE, designated SEQ ID:8979, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36751] Another function of VGAM992 is therefore inhibition of Sialyltransferase 4A (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM_003033). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT4A. Stromal Antigen 3 (STAG3, Accession NM_012447) is another VGAM992 host target gene. STAG3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STAG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAG3 BINDING SITE, designated SEQ ID:14819, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36752] Another function of VGAM992 is therefore inhibition of Stromal Antigen 3 (STAG3, Accession NM_012447). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAG3. Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM_014820) is another VGAM992 host target gene. TOMM70A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOMM70A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOMM70A BINDING SITE, designated SEQ ID:16789, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36753] Another function of VGAM992 is therefore inhibition of Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM_014820). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOMM70A. LOC138241 (Accession XM_059957) is another VGAM992 host target gene.

LOC138241 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138241 BINDING SITE, designated SEQ ID:37120, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36754] Another function of VGAM992 is therefore inhibition of LOC138241 (Accession XM_059957). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138241. LOC144848 (Accession XM_056770) is another VGAM992 host target gene. LOC144848 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144848 BINDING SITE, designated SEQ ID:36420, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36755] Another function of VGAM992 is therefore inhibition of LOC144848 (Accession XM_056770). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144848. LOC170395 (Accession XM_084325) is another VGAM992 host target gene. LOC170395 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170395 BINDING SITE, designated SEQ ID:37544, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36756] Another function of VGAM992 is therefore inhibition of LOC170395 (Accession XM_084325). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170395. LOC220575 (Accession XM_083991) is another VGAM992 host target gene. LOC220575 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220575, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220575 BINDING SITE, designated SEQ ID:37529, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36757] Another function of VGAM992 is therefore inhibition of LOC220575 (Accession XM_083991). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220575. LOC254181 (Accession XM_174526) is another VGAM992 host target gene. LOC254181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254181 BINDING SITE, designated SEQ ID:46597, to the nucleotide sequence of VGAM992 RNA, herein designated VGAM RNA, also designated SEQ ID:3703.

[36758] Another function of VGAM992 is therefore inhibition of LOC254181 (Accession XM_174526). Accordingly, utilities of VGAM992 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC254181. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 993 (VGAM993) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36759] VGAM993 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM993 was detected is described hereinabove with reference to Figs. 1–8.

[36760] VGAM993 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36761] VGAM993 gene encodes a VGAM993 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM993 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM993 precursor RNA is designated SEQ ID:979, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:979 is located at position 4662 relative to the genome of Leishmania RNA Virus 1-1.

[36762] VGAM993 precursor RNA folds onto itself, forming VGAM993 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36763] An enzyme complex designated DICER COMPLEX, `dices` the VGAM993 folded precursor RNA into VGAM993 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM993 RNA is designated SEQ ID:3704, and is provided hereinbelow with reference to the sequence listing part.

[36764] VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM993 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36765] VGAM993 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM993 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM993 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36766] The complementary binding of VGAM993 RNA, herein designated VGAM RNA, to host target binding sites on VGAM993 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM993 host target RNA into VGAM993 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36767] It is appreciated that VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM993 host target genes. The mRNA of each one of this plurality of VGAM993 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM993 RNA, herein designated VGAM RNA, and which when bound by VGAM993 RNA causes in-

hibition of translation of respective one or more VGAM993 host target proteins.

[36768] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM993 gene, herein designated VGAM GENE, on one or more VGAM993 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36769] It is yet further appreciated that a function of VGAM993 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM993 include diagnosis, prevention and

treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM993 correlate with, and may be deduced from, the identity of the host target genes which VGAM993 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36770] Nucleotide sequences of the VGAM993 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM993 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM993 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM993 are further described hereinbelow with reference to Table 1.

[36771] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM993 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM993 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36772] As mentioned hereinabove with reference to Fig. 1, a function of VGAM993 gene, herein designated VGAM is inhibition of expression of VGAM993 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM993 correlate with, and may be deduced from, the identity of the target genes which VGAM993 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36773] Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455) is a VGAM993 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10751, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36774] A function of VGAM993 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM806. Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823) is another VGAM993 host target gene. PKIA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PKIA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIA BINDING SITE, designated SEQ ID:13699, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36775] Another function of VGAM993 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIA. PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_015866) is another VGAM993 host target gene. PRDM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE, designated SEQ ID:18005, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36776] Another function of VGAM993 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_015866), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884) is another VGAM993 host target gene. RAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP1A BINDING SITE, designated SEQ

ID:8794, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36777] Another function of VGAM993 is therefore inhibition of RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884), a gene which induces morphological reversion of a cell line transformed by a ras oncogene. Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP1A. The function of RAP1A has been established by previous studies. Three human cDNAs encoding 'new' RAS-related proteins, designated RAP1A, RAP1B, and RAP2, were isolated by Pizon et al. (1988). These proteins share approximately 50% amino acid identity with the classical RAS proteins and have numerous structural features in common. The most striking difference between the RAP and RAS proteins resides in their 61st amino acid: glutamine in RAS is replaced by threonine in RAP proteins. Animal model experiments lend further support to the function of RAP1A. Using mice transgenic for constitutive expression of Rap1a within the T cell lineage, Sebzda et al. (2002) found that instead of anergy, these T cells showed enhanced T cell receptor-me-

diated responses, both in thymocytes and in mature T cells. In addition, Rap1a activation induces strong activation of beta-1 (OMIM Ref. No. 135630) and beta-2 (OMIM Ref. No. 600065) integrins. The authors concluded that Rap1a positively influences T cells by augmenting their responses and directing integrin activation.

[36778] It is appreciated that the abovementioned animal model for RAP1A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[36779] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36780] Pizon, V.; Chardin, P.; Lerosey, I.; Olofsson, B.; Tavitian, A. : Human cDNAs RAP1 and RAP2 homologous to the Drosophila gene Dras3 encode proteins closely related to ras in the 'effector' region. *Oncogene* 3: 201-204, 1988. ; and

[36781] Kitayama, H.; Sugimoto, Y.; Matsuzaki, T.; Ikawa, Y.; Noda, M. : A ras-related gene with transformation suppressor activity. *Cell* 56: 77-84, 1989. PubMed ID : 2642744 9. Sebzda, E.; Brac.

[36782] Further studies establishing the function and utilities of

RAP1A are found in John Hopkins OMIM database record ID 179520, and in cited publications numbered 2547–2550, 1184, 488 and 12377–12381 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380) is another VGAM993 host target gene. DDX28 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DDX28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX28 BINDING SITE, designated SEQ ID:20408, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36783] Another function of VGAM993 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX28. Potassium Voltage–gated Channel, Shal–related Subfamily, Member 1 (KCND1, Accession NM_004979) is another VGAM993 host target gene. KCND1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by KCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND1 BINDING SITE, designated SEQ ID:11424, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36784] Another function of VGAM993 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM_004979). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCND1. MGC13251 (Accession NM_032714) is another VGAM993 host target gene. MGC13251 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13251 BINDING SITE, designated SEQ ID:26436, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36785] Another function of VGAM993 is therefore inhibition of MGC13251 (Accession NM_032714). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13251. Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202) is another VGAM993 host target gene. SS18L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SS18L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS18L1 BINDING SITE, designated SEQ ID:32558, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36786] Another function of VGAM993 is therefore inhibition of Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18L1. LOC124460 (Accession XM_071892) is another VGAM993 host target gene. LOC124460 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC124460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124460 BINDING SITE, designated SEQ ID:37445, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36787] Another function of VGAM993 is therefore inhibition of LOC124460 (Accession XM_071892). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124460. LOC138130 (Accession XM_070771) is another VGAM993 host target gene. LOC138130 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138130 BINDING SITE, designated SEQ ID:37394, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36788] Another function of VGAM993 is therefore inhibition of LOC138130 (Accession XM_070771). Accordingly, utilities

of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138130. LOC152620 (Accession XM_011108) is another VGAM993 host target gene. LOC152620 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152620 BINDING SITE, designated SEQ ID:30173, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36789] Another function of VGAM993 is therefore inhibition of LOC152620 (Accession XM_011108). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152620. LOC158668 (Accession XM_045161) is another VGAM993 host target gene. LOC158668 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC158668 BINDING SITE, designated SEQ ID:34377, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36790] Another function of VGAM993 is therefore inhibition of LOC158668 (Accession XM_045161). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158668. LOC254312 (Accession XM_172839) is another VGAM993 host target gene. LOC254312 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254312 BINDING SITE, designated SEQ ID:46113, to the nucleotide sequence of VGAM993 RNA, herein designated VGAM RNA, also designated SEQ ID:3704.

[36791] Another function of VGAM993 is therefore inhibition of LOC254312 (Accession XM_172839). Accordingly, utilities of VGAM993 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254312. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 994 (VGAM994) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36792] VGAM994 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM994 was detected is described hereinabove with reference to Figs. 1–8.

[36793] VGAM994 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36794] VGAM994 gene encodes a VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM994 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM994 precursor RNA is designated SEQ ID:980, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:980 is located at position 4299 relative to the genome of Leish-

mania RNA Virus 1-1.

[36795] VGAM994 precursor RNA folds onto itself, forming VGAM994 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36796] An enzyme complex designated DICER COMPLEX, `dices` the VGAM994 folded precursor RNA into VGAM994 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM994 RNA is designated SEQ ID:3705, and is provided hereinbelow with reference to the sequence listing part.

[36797] VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM994 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36798] VGAM994 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM994 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM994 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36799] The complementary binding of VGAM994 RNA, herein designated VGAM RNA, to host target binding sites on VGAM994 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM994 host target RNA into VGAM994 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36800] It is appreciated that VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM994 host target genes. The mRNA of each one of this plurality of VGAM994 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM994 RNA, herein designated VGAM RNA, and which when bound by VGAM994 RNA causes inhibition of translation of respective one or more VGAM994 host target proteins.

[36801] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM994 gene, herein designated VGAM GENE, on one or more VGAM994 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36802] It is yet further appreciated that a function of VGAM994 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM994

correlate with, and may be deduced from, the identity of the host target genes which VGAM994 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36803] Nucleotide sequences of the VGAM994 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM994 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM994 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM994 are further described hereinbelow with reference to Table 1.

[36804] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM994 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM994 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36805] As mentioned hereinabove with reference to Fig. 1, a function of VGAM994 gene, herein designated VGAM is inhibition of expression of VGAM994 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM994 correlate with, and may be deduced

from, the identity of the target genes which VGAM994 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36806] Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM_012193) is a VGAM994 host target gene. FZD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD4 BINDING SITE, designated SEQ ID:14489, to the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, also designated SEQ ID:3705.

[36807] A function of VGAM994 is therefore inhibition of Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM_012193), a gene which may function in cell polarity, cell fate specification and cancer; similar to frizzled receptor family, has seven transmembrane domains. Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD4. The function of FZD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM309.Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983) is another VGAM994 host target gene.

SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10131, to the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, also designated SEQ ID:3705.

[36808] Another function of VGAM994 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87.FLJ10932 (Accession NM_018277) is another VGAM994 host target

gene. FLJ10932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10932 BINDING SITE, designated SEQ ID:20264, to the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, also designated SEQ ID:3705.

[36809] Another function of VGAM994 is therefore inhibition of FLJ10932 (Accession NM_018277). Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10932. KIAA1906 (Accession XM_055095) is another VGAM994 host target gene. KIAA1906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1906 BINDING SITE, designated SEQ ID:36230, to the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, also designated SEQ ID:3705.

[36810] Another function of VGAM994 is therefore inhibition of KIAA1906 (Accession XM_055095). Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1906. LOC126917 (Accession XM_059091) is another VGAM994 host target gene. LOC126917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE, designated SEQ ID:36870, to the nucleotide sequence of VGAM994 RNA, herein designated VGAM RNA, also designated SEQ ID:3705.

[36811] Another function of VGAM994 is therefore inhibition of LOC126917 (Accession XM_059091). Accordingly, utilities of VGAM994 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126917. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 995 (VGAM995) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[36812] VGAM995 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM995 was detected is described hereinabove with reference to Figs. 1–8.

[36813] VGAM995 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36814] VGAM995 gene encodes a VGAM995 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM995 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM995 precursor RNA is designated SEQ ID:981, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:981 is located at position 4489 relative to the genome of Leishmania RNA Virus 1–1.

[36815] VGAM995 precursor RNA folds onto itself, forming VGAM995 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36816] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM995 folded precursor RNA into VGAM995 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 43%) nucleotide se-
quence of VGAM995 RNA is designated SEQ ID:3706, and
is provided hereinbelow with reference to the sequence
listing part.

[36817] VGAM995 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM995 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM995 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36818] VGAM995 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM995 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM995 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36819] The complementary binding of VGAM995 RNA, herein designated VGAM RNA, to host target binding sites on VGAM995 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM995 host target RNA into VGAM995 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36820] It is appreciated that VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM995 host target genes. The mRNA of each one of this plurality of VGAM995 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM995 RNA, herein designated VGAM RNA, and which when bound by VGAM995 RNA causes inhibition of translation of respective one or more VGAM995 host target proteins.

[36821] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM995 gene, herein designated VGAM GENE, on one or more VGAM995 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36822] It is yet further appreciated that a function of VGAM995 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM995 correlate with, and may be deduced from, the identity of the host target genes which VGAM995 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [36823] Nucleotide sequences of the VGAM995 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM995 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM995 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM995 are further described hereinbelow with reference to Table 1.
- [36824] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM995 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM995 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36825] As mentioned hereinabove with reference to Fig. 1, a function of VGAM995 gene, herein designated VGAM is inhibition of expression of VGAM995 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM995 correlate with, and may be deduced from, the identity of the target genes which VGAM995 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36826] Aryl Hydrocarbon Receptor (AHR, Accession NM_001621) is a VGAM995 host target gene. AHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AHR BINDING SITE, designated SEQ ID:7335, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36827] A function of VGAM995 is therefore inhibition of Aryl Hydrocarbon Receptor (AHR, Accession NM_001621), a gene which plays a role in modulating carcinogenesis through the induction of xenobiotic-metabolizing enzymes. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AHR. The function of AHR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM368.ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933) is another VGAM995 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32509, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36828] Another function of VGAM995 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. B-cell CLL/lymphoma 2 (BCL2, Accession NM_000633) is another VGAM995 host target gene. BCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2 BINDING SITE, designated SEQ ID:6262, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36829] Another function of VGAM995 is therefore inhibition of B-

cell CLL/lymphoma 2 (BCL2, Accession NM_000633). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2. Calcitonin Receptor-like (CALCRL, Accession NM_005795) is another VGAM995 host target gene. CALCRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALCRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALCRL BINDING SITE, designated SEQ ID:12376, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36830] Another function of VGAM995 is therefore inhibition of Calcitonin Receptor-like (CALCRL, Accession NM_005795), a gene which is a receptor for calcitonin gene-related peptide type 1. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALCRL. The function of CALCRL has been established by previous studies. McLatchie et al. (1998) demonstrated that a complex consisting of RAMP2 and CALCRL can function as an ADM re-

ceptor. To investigate whether ADM has implications as a pathophysiologic substance in pregnancy-induced hypertension, Makino et al. (2001) measured the changes of expression of RAMP2 and CALCRL in fetomaternal tissues in normotensive pregnant women and pregnancy-induced hypertensive women by Northern blot analysis. RAMP2 and CALCRL mRNA was significantly decreased in the umbilical artery and uterus of the patients with pregnancy-induced hypertension. On the other hand, RAMP2 mRNA was significantly increased in the fetal membrane of the patients with pregnancy-induced hypertension. In addition, there was a significant negative correlation between the RAMP2 mRNA levels in the umbilical artery and uterine muscle and blood pressure. However, there was no correlation between the mRNA level and blood pressure in fetal membrane and placenta, suggesting that there is no close relationship to the pathogenesis in pregnancy-induced hypertension. These findings suggested that the reduced expression of RAMP2 and CALCRL functioning as components of an adrenomedullin receptor in umbilical artery and uterus may have some role in pregnancy-induced hypertension. In a mammalian cell line without an endogenous receptor, McLatchie et al. (1998) observed increased

intracellular cAMP levels in response to CGRP when CGRPR and receptor activity-modifying protein-1 (RAMP1; 605153) were expressed together, but not when they were expressed alone. Flow cytometric analysis showed that expression of CGRPR at the cell surface increases substantially when CGRPR is expressed with RAMP1. Likewise, surface expression of RAMP1 was shown to increase in cells also expressing CGRPR. SDS-PAGE analysis showed that binding of CGRP requires expression of both the 14-kD RAMP1 and the 58-kD CGRPR glycoprotein. The authors demonstrated that in the presence of RAMP1, CGRPR becomes a 66-kD terminally glycosylated protein. McLatchie et al. (1998) found that unlike RAMP1, RAMP2 (OMIM Ref. No. 605154) and RAMP3 (OMIM Ref. No. 605155) do not potentiate responses to CGRP but do transport the glycosylated 58-kD but not the 66-kD form of CGRPR to the cell surface. In frog oocytes and mammalian cells, coexpression of RAMP2 and CGRPR resulted in increased intracellular cAMP concentrations in response to ADM but not to CGRP, CT, or IAPP. SDS-PAGE analysis demonstrated that ADM binds to coexpressed RAMP2 and CGRPR. McLatchie et al. (1998) demonstrated that a complex consisting of RAMP2 and CALCRL can function as an

ADM receptor. To investigate whether ADM has implications as a pathophysiologic substance in pregnancy-induced hypertension, Makino et al. (2001) measured the changes of expression of RAMP2 and CALCRL in fetomaternal tissues in normotensive pregnant women and pregnancy-induced hypertensive women by Northern blot analysis. RAMP2 and CALCRL mRNA was significantly decreased in the umbilical artery and uterus of the patients with pregnancy-induced hypertension. On the other hand, RAMP2 mRNA was significantly increased in the fetal membrane of the patients with pregnancy-induced hypertension. In addition, there was a significant negative correlation between the RAMP2 mRNA levels in the umbilical artery and uterine muscle and blood pressure. However, there was no correlation between the mRNA level and blood pressure in fetal membrane and placenta, suggesting that there is no close relationship to the pathogenesis in pregnancy-induced hypertension. These findings suggested that the reduced expression of RAMP2 and CALCRL functioning as components of an adrenomedullin receptor in umbilical artery and uterus may have some role in pregnancy-induced hypertension.

[36831] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [36832] McLatchie, L. M.; Fraser, N. J.; Main, M. J.; Wise, A.; Brown, J.; Thompson, N.; Solari, R.; Lee, M. G.; Foord, S. M. : RAMPs regulate the transport and ligand specificity of the calcitonin–receptor–like receptor. *Nature* 393: 333–339, 1998. ; and
- [36833] Makino, Y.; Shibata, K.; Makino, I.; Kangawa, K.; Kawarabayashi, T. : Alteration of the adrenomedullin receptor components gene expression associated with the blood pressure in pregnancy.
- [36834] Further studies establishing the function and utilities of CALCRL are found in John Hopkins OMIM database record ID 114190, and in cited publications numbered 4693–4697, 4301–430 and 4698 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calpain 10 (CAPN10, Accession NM_023088) is another VGAM995 host target gene. CAPN10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CAPN10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CAPN10 BINDING SITE, designated SEQ ID:23355, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36835] Another function of VGAM995 is therefore inhibition of Calpain 10 (CAPN10, Accession NM_023088), a gene which catalyzes limited proteolysis of substrates involved in cytoskeletal remodelling and signal transduction. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN10. The function of CAPN10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. CRACC (Accession NM_021181) is another VGAM995 host target gene. CRACC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRACC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRACC BINDING SITE, designated SEQ ID:22156, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ

ID:3706.

[36836] Another function of VGAM995 is therefore inhibition of CRACC (Accession NM_021181), a gene which may participate in adhesion reactions between T lymphocytes and accessory cells. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRACC. The function of CRACC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM26. Fas (TNFRSF6)-associated Via Death Domain (FADD, Accession NM_003824) is another VGAM995 host target gene. FADD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FADD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FADD BINDING SITE, designated SEQ ID:9918, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36837] Another function of VGAM995 is therefore inhibition of Fas (TNFRSF6)-associated Via Death Domain (FADD, Accession NM_003824), a gene which may play an important

role in the proximal signal transduction of FAS. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FADD. The function of FADD has been established by previous studies. FADD is a universal adapter protein in apoptosis that mediates signaling of all known death domain-containing members of the TNF receptor superfamily (Kabra et al., 2001). Animal model experiments lend further support to the function of FADD. Yeh et al. (1998) found that FAS (CD95), TNFR1, and death receptor 3 (OMIM Ref. No. 603366) did not induce apoptosis in FADD-deficient embryonic fibroblasts, whereas DR4, oncogenes E1A and c-myc (OMIM Ref. No. 190080), and chemotherapeutic agent adriamycin did. Mice with a deletion in the FADD gene did not survive beyond day 11.5 of embryogenesis; these mice showed signs of cardiac failure and abdominal hemorrhage. Chimeric embryos showing a high contribution of FADD-null mutant cells to the heart reproduced the phenotype of FADD-deficient mutants. Thus, not only death receptors but also receptors that couple to developmental programs may use FADD for signaling. Since FAS is necessary for homeostasis in the immune system, Zhang et al. (1998) investigated the ef-

fect of FADD deletion in lymphoid organs. Since FADD-null mice die in utero, they used FADD-null, RAG1 (OMIM Ref. No. 179615)-null chimeras in which all mature lymphocytes were derived from the FADD-null cells, as RAG1-null mice are not capable of producing B or T cells. FAS-induced apoptosis was completely blocked in thymocytes from the FADD-null mice, indicating that there are no redundant FAS apoptotic pathways. Although thymocyte subpopulations were apparently normal in newborn chimeras, the thymocytes decreased to undetectable levels as these mice age. Peripheral T cells were present in all older FADD-null chimeras, but activation-induced proliferation was impaired despite production of IL2 (OMIM Ref. No. 147680). These results and the similarities between FADD-null mice and mice lacking the beta-subunits of the IL2 receptor (IL2RB; 146710), suggested to Zhang et al. (1998) that there is an unexpected connection between cell proliferation and apoptosis.

[36838] It is appreciated that the abovementioned animal model for FADD is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[36839] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [36840] Chinnaiyan, A. M.; O'Rourke, K.; Tewari, M.; Dixit, V. M. : FADD, a novel death domain-containing protein, interacts with the death domain of Fas and initiates apoptosis. *Cell* 81: 505–512, 1995. ; and
- [36841] Zhang, J.; Cado, D.; Chen, A.; Kabra, N. H.; Winoto, A. : Fas-mediated apoptosis and activation-induced T-cell proliferation are defective in mice lacking FADD/Mort1. *Nature* 392: 296–300.
- [36842] Further studies establishing the function and utilities of FADD are found in John Hopkins OMIM database record ID 602457, and in cited publications numbered 6325–6326, 596 and 6184–6185 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876) is another VGAM995 host target gene. IGF2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGF2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2R BINDING SITE, designated SEQ ID:6558,

to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36843] Another function of VGAM995 is therefore inhibition of Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876), a gene which transport of phosphorylated lysosomal enzymes from the golgi complex and the cell surface to lysosomes. lysosomal enzymes bearing phosphomannosyl residues bind specifically to mannose-6-phosphate receptors in the golgi apparatus and the resulting receptor-ligand complex is transported to an acidic prelysosomal compartment where the low ph mediates the dissociation of the complex. this receptor also binds insulin growth factor ii. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2R. The function of IGF2R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM209. Loss of Heterozygosity, 11, Chromosomal Region 2, Gene A (LOH11CR2A, Accession NM_014622) is another VGAM995 host target gene. LOH11CR2A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOH11CR2A, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOH11CR2A BINDING SITE, designated SEQ ID:15986, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36844] Another function of VGAM995 is therefore inhibition of Loss of Heterozygosity, 11, Chromosomal Region 2, Gene A (LOH11CR2A, Accession NM_014622). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOH11CR2A. Snail Homolog 1 (Drosophila) (SNAI1, Accession NM_005985) is another VGAM995 host target gene. SNAI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAI1 BINDING SITE, designated SEQ ID:12606, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36845] Another function of VGAM995 is therefore inhibition of Snail Homolog 1 (Drosophila) (SNAI1, Accession

NM_005985). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAI1. Sulfotransferase Family, Cytosolic, 1A, Phenol-preferring, Member 2 (SULT1A2, Accession XM_051068) is another VGAM995 host target gene. SULT1A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SULT1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT1A2 BINDING SITE, designated SEQ ID:35734, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36846] Another function of VGAM995 is therefore inhibition of Sulfotransferase Family, Cytosolic, 1A, Phenol-preferring, Member 2 (SULT1A2, Accession XM_051068), a gene which catalyzes the sulfate conjugation of target proteins and mediates the metabolic activation of carcinogenic n-hydroxyarylamines. Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT1A2. The function of SULT1A2 has been established by previous studies.

Sulfonation is an important pathway in the biotransformation of many drugs, xenobiotics, neurotransmitters, and steroid hormones. The thermostable form of phenol sulfotransferase preferentially catalyzes the sulfonation of 'simple' planar phenols. The phenol sulfotransferase STP1 (OMIM Ref. No. 171150) maps to chromosome 16. Her et al. (1996) determined the structure and chromosomal localization of the gene encoding a second phenol sulfotransferase, STP2. The gene spans approximately 5.1 kb and contains 9 exons that range in length from 74 to 347 bp. The locations of most STP2 exon/intron splice junctions are identical to those of a gene for the thermolabile form of PST in humans, STM (OMIM Ref. No. 600641), which maps to 16p close to the location of the thermostable STP1. Her et al. (1996) mapped STP2 to human chromosome 16 by PCR with DNA from human/rodent somatic cell hybrids. Dooley and Huang (1996) determined the genomic organization of the human STP1, STP2, and STM (OMIM Ref. No. 600641) genes. These 3 genes each have 8 exons with the initiator methionine on exon 2. All 3 colocalize on a single cosmid from chromosome 16p12.1–p11.2 and have a high degree of sequence homology, suggesting that these 3 genes arose by gene du-

plication. Dooley and Huang (1996) stated that the previously identified PST gene sequences HAST4, HAST4v, and ST1A2 are isolates of the STP2 gene.

[36847] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36848] Dooley, T. P.; Huang, Z. : Genomic organization and DNA sequences of two human phenol sulfotransferase genes (STP1 and STP2) on the short arm of chromosome 16. Biochem. Biophys. Res. Commun. 228: 134–140, 1996. ; and

[36849] Her, C.; Raftogianis, R.; Weinshilboum, R. M. : Human phenol sulfotransferase STP2 gene: molecular cloning, structural characterization, and chromosomal localization. Genomics 33: 409–4.

[36850] Further studies establishing the function and utilities of SULT1A2 are found in John Hopkins OMIM database record ID 601292, and in cited publications numbered 5264–5265 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ankyrin Repeat and SOCS Box–containing 13 (ASB13, Accession NM_024701) is another VGAM995 host target gene. ASB13 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by ASB13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASB13 BINDING SITE, designated SEQ ID:24012, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36851] Another function of VGAM995 is therefore inhibition of Ankyrin Repeat and SOCS Box-containing 13 (ASB13, Accession NM_024701). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASB13. DKFZP434C1715 (Accession XM_098421) is another VGAM995 host target gene. DKFZP434C1715 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434C1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C1715 BINDING SITE, designated SEQ ID:41676, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ

ID:3706.

[36852] Another function of VGAM995 is therefore inhibition of DKFZP434C1715 (Accession XM_098421). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C1715. FLJ10604 (Accession NM_018154) is another VGAM995 host target gene. FLJ10604 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10604, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10604 BINDING SITE, designated SEQ ID:19964, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36853] Another function of VGAM995 is therefore inhibition of FLJ10604 (Accession NM_018154). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10604. FLJ10898 (Accession XM_002486) is another VGAM995 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29889, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36854] Another function of VGAM995 is therefore inhibition of FLJ10898 (Accession XM_002486). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. KIAA0721 (Accession XM_171125) is another VGAM995 host target gene. KIAA0721 BINDING SITE1 and KIAA0721 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0721, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0721 BINDING SITE1 and KIAA0721 BINDING SITE2, designated SEQ ID:45925 and SEQ ID:22318 respectively, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36855] Another function of VGAM995 is therefore inhibition of KIAA0721 (Accession XM_171125). Accordingly, utilities

of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0721. KIAA1091 (Accession XM_045750) is another VGAM995 host target gene. KIAA1091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1091 BINDING SITE, designated SEQ ID:34539, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36856] Another function of VGAM995 is therefore inhibition of KIAA1091 (Accession XM_045750). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1091. MGC4266 (Accession NM_032680) is another VGAM995 host target gene. MGC4266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4266

BINDING SITE, designated SEQ ID:26401, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36857] Another function of VGAM995 is therefore inhibition of MGC4266 (Accession NM_032680). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4266. Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM_002816) is another VGAM995 host target gene. PSMD12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMD12 BINDING SITE, designated SEQ ID:8681, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36858] Another function of VGAM995 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 12 (PSMD12, Accession NM_002816). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with PSMD12. Regulatory Factor X, 4 (influences HLA class II expression) (RFX4, Accession NM_032491) is another VGAM995 host target gene. RFX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX4 BINDING SITE, designated SEQ ID:26242, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36859] Another function of VGAM995 is therefore inhibition of Regulatory Factor X, 4 (influences HLA class II expression) (RFX4, Accession NM_032491). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX4. LOC118709 (Accession XM_058338) is another VGAM995 host target gene. LOC118709 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC118709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118709 BINDING

SITE, designated SEQ ID:36598, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36860] Another function of VGAM995 is therefore inhibition of LOC118709 (Accession XM_058338). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118709. LOC126669 (Accession XM_060121) is another VGAM995 host target gene. LOC126669 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126669 BINDING SITE, designated SEQ ID:37159, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36861] Another function of VGAM995 is therefore inhibition of LOC126669 (Accession XM_060121). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126669. LOC138241 (Accession XM_059957) is another VGAM995 host target gene. LOC138241 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138241 BINDING SITE, designated SEQ ID:37121, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36862] Another function of VGAM995 is therefore inhibition of LOC138241 (Accession XM_059957). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138241. LOC145900 (Accession XM_085276) is another VGAM995 host target gene. LOC145900 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145900 BINDING SITE, designated SEQ ID:38012, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36863] Another function of VGAM995 is therefore inhibition of

LOC145900 (Accession XM_085276). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145900. LOC149844 (Accession XM_086675) is another VGAM995 host target gene. LOC149844 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149844, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149844 BINDING SITE, designated SEQ ID:38823, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36864] Another function of VGAM995 is therefore inhibition of LOC149844 (Accession XM_086675). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149844. LOC151438 (Accession XM_098060) is another VGAM995 host target gene. LOC151438 BINDING SITE1 and LOC151438 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC151438, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151438 BINDING SITE1 and LOC151438 BINDING SITE2, designated SEQ ID:41346 and SEQ ID:41350 respectively, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36865] Another function of VGAM995 is therefore inhibition of LOC151438 (Accession XM_098060). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151438. LOC157376 (Accession XM_088301) is another VGAM995 host target gene. LOC157376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157376 BINDING SITE, designated SEQ ID:39601, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36866] Another function of VGAM995 is therefore inhibition of LOC157376 (Accession XM_088301). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC157376. LOC197342 (Accession XM_113869) is another VGAM995 host target gene. LOC197342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197342 BINDING SITE, designated SEQ ID:42489, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36867] Another function of VGAM995 is therefore inhibition of LOC197342 (Accession XM_113869). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197342. LOC203286 (Accession XM_117526) is another VGAM995 host target gene. LOC203286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43497, to

the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36868] Another function of VGAM995 is therefore inhibition of LOC203286 (Accession XM_117526). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. LOC222614 (Accession XM_169970) is another VGAM995 host target gene. LOC222614 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222614 BINDING SITE, designated SEQ ID:45306, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36869] Another function of VGAM995 is therefore inhibition of LOC222614 (Accession XM_169970). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222614. LOC253613 (Accession XM_171225) is another VGAM995 host target gene. LOC253613 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC253613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253613 BINDING SITE, designated SEQ ID:46013, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36870] Another function of VGAM995 is therefore inhibition of LOC253613 (Accession XM_171225). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253613. LOC254936 (Accession XM_170770) is another VGAM995 host target gene. LOC254936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254936 BINDING SITE, designated SEQ ID:45527, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36871] Another function of VGAM995 is therefore inhibition of LOC254936 (Accession XM_170770). Accordingly, utilities

of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254936. LOC255870 (Accession XM_170628) is another VGAM995 host target gene. LOC255870 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255870 BINDING SITE, designated SEQ ID:45406, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36872] Another function of VGAM995 is therefore inhibition of LOC255870 (Accession XM_170628). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255870. LOC51336 (Accession NM_016646) is another VGAM995 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC51336 BINDING SITE, designated SEQ ID:18753, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36873] Another function of VGAM995 is therefore inhibition of LOC51336 (Accession NM_016646). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51336. LOC58486 (Accession NM_021211) is another VGAM995 host target gene. LOC58486 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC58486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58486 BINDING SITE, designated SEQ ID:22187, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36874] Another function of VGAM995 is therefore inhibition of LOC58486 (Accession NM_021211). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58486. LOC89135 (Accession XM_016232) is another VGAM995 host target gene. LOC89135 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89135 BINDING SITE, designated SEQ ID:30250, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36875] Another function of VGAM995 is therefore inhibition of LOC89135 (Accession XM_016232). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89135. LOC90538 (Accession XM_032401) is another VGAM995 host target gene. LOC90538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90538 BINDING SITE, designated SEQ ID:31658, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36876] Another function of VGAM995 is therefore inhibition of

LOC90538 (Accession XM_032401). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90538. LOC91974 (Accession XM_041974) is another VGAM995 host target gene. LOC91974 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91974, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91974 BINDING SITE, designated SEQ ID:33651, to the nucleotide sequence of VGAM995 RNA, herein designated VGAM RNA, also designated SEQ ID:3706.

[36877] Another function of VGAM995 is therefore inhibition of LOC91974 (Accession XM_041974). Accordingly, utilities of VGAM995 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91974. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 996 (VGAM996) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[36878] VGAM996 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM996 was detected is described hereinabove with reference to Figs. 1–8.

[36879] VGAM996 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Leishmania RNA Virus 1–1. VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36880] VGAM996 gene encodes a VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM996 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM996 precursor RNA is designated SEQ ID:982, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:982 is located at position 3625 relative to the genome of Leishmania RNA Virus 1–1.

[36881] VGAM996 precursor RNA folds onto itself, forming VGAM996 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[36882] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM996 folded precursor RNA into VGAM996 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 44%) nucleotide se-
quence of VGAM996 RNA is designated SEQ ID:3707, and
is provided hereinbelow with reference to the sequence
listing part.

[36883] VGAM996 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM996 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM996 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[36884] VGAM996 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM996 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM996 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5' UTR regions.

[36885] The complementary binding of VGAM996 RNA, herein designated VGAM RNA, to host target binding sites on VGAM996 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM996 host target RNA into VGAM996 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36886] It is appreciated that VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM996 host target genes. The mRNA of each one of this plurality of VGAM996 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM996 RNA, herein designated VGAM RNA, and which when bound by VGAM996 RNA causes inhibition of translation of respective one or more VGAM996 host target proteins.

[36887] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM996 gene, herein designated VGAM GENE, on one or

more VGAM996 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36888] It is yet further appreciated that a function of VGAM996 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGAM996 correlate with, and may be deduced from, the identity of the host target genes which VGAM996 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [36889] Nucleotide sequences of the VGAM996 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM996 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM996 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM996 are further described hereinbelow with reference to Table 1.
- [36890] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM996 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM996 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36891] As mentioned hereinabove with reference to Fig. 1, a function of VGAM996 gene, herein designated VGAM is inhibition of expression of VGAM996 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM996 correlate with, and may be deduced from, the identity of the target genes which VGAM996 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [36892] V-raf Murine Sarcoma 3611 Viral Oncogene Homolog 1

(ARAF1, Accession XM_033884) is a VGAM996 host target gene. ARAF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARAF1 BINDING SITE, designated SEQ ID:31980, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36893] A function of VGAM996 is therefore inhibition of V-raf Murine Sarcoma 3611 Viral Oncogene Homolog 1 (ARAF1, Accession XM_033884), a gene which may play a critical role in cell growth and development. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARAF1. The function of ARAF1 has been established by previous studies. By screening a mouse cDNA library with a v-raf oncogene probe, Huebner et al. (1986) also isolated a transforming raf-related cDNA, A-raf, that represented a gene distinct from RAF1. As an initial step in the analysis of this RAF1-related cDNA, they isolated a human ARAF cDNA and used it to map the genes in mouse and man.

The mouse gene cosegregated with the X chromosome in Chinese hamster–mouse hybrid cells. In humans, 2 independently segregating loci, designated ARAF1 and ARAF2, were mapped to chromosomes X and 7, respectively.

(Huebner et al. (1986) had not conclusively shown that the ARAF2 locus on chromosome 7 is transcribed, and indeed the ARAF2 locus, now designated ARAF2P, has been shown to be a pseudogene (Lee et al., 1994).) The single X-linked ARAF locus of the mouse and the ARAF1 locus of man are actively transcribed in several mouse and human cell lines. Because of an 80% homology to RAF1 in its kinase domain, the authors speculated that the ARAF1 gene product may have serine/threonine-specific kinase activity. By in situ hybridization, ARAF1 was mapped to Xp21–q11, probably Xp13–p11. Popescu and Mark (1989) regionalized the gene to Xp11.4–p11.2 by in situ hybridization. Beck et al. (1987) deduced the complete 606–amino acid sequence of the human ARAF1 oncogene from the 2,453–nucleotide sequence of the cDNA. Avner et al. (1987) found that in the mouse the A-raf oncogene is on the X chromosome, 10 to 17 cM proximal to the Hprt gene. The localization was considered compatible with the presence of the ARAF oncogene on the short arm

of the X chromosome between the centromere and Xp21 in man. The RAF protooncogenes encode cytoplasmic protein serine/threonine kinases that play a critical role in cell growth and development. Araf1 in the mouse is expressed predominantly in urogenital tissues. Lee et al. (1994) demonstrated that the ARAF1 gene in the human comprises 16 exons encoded by a minimum of 10,776 nucleotides.

[36894] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36895] Beck, T. W.; Huleihel, M.; Gunnell, M.; Bonner, T. I.; Rapp, U. R. : The complete coding sequence of the human A-raf-1 oncogene and transforming activity of a human A-raf carrying retrovirus. Nucleic Acids Res. 15: 595-609, 1987. ; and

[36896] Lee, J.-E.; Beck, T. W.; Brennscheidt, U.; DeGennaro, L. J.; Rapp, U. R. : The complete sequence and promoter activity of the human A-raf-1 gene (ARAF1). Genomics 20: 43-55, 1994.

[36897] Further studies establishing the function and utilities of ARAF1 are found in John Hopkins OMIM database record ID 311010, and in cited publications numbered

8382–8387 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CARPX (Accession NM_020178) is another VGAM996 host target gene. CARPX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CARPX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARPX BINDING SITE, designated SEQ ID:21393, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36898] Another function of VGAM996 is therefore inhibition of CARPX (Accession NM_020178), a gene which is alpha-carbonic anhydrases-related protein. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARPX. The function of CARPX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM904.RP42 (Accession NM_020640) is another VGAM996 host target gene. RP42 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by RP42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP42 BINDING SITE, designated SEQ ID:21799, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36899] Another function of VGAM996 is therefore inhibition of RP42 (Accession NM_020640), a gene which not clear yet. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP42. The function of RP42 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM47. Sarcospan (Kras oncogene-associated gene) (SSPN, Accession NM_005086) is another VGAM996 host target gene. SSPN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSPN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSPN BINDING SITE, designated SEQ ID:11535, to the nucleotide se-

quence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36900] Another function of VGAM996 is therefore inhibition of Sarcospan (Kras oncogene-associated gene) (SSPN, Accession NM_005086), a gene which spans the muscle plasma membrane and forms a link between the f-actin cytoskeleton and the extracellular matrix. Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSPN. The function of SSPN has been established by previous studies. Scott et al. (1994) reported the sequence of a gene in mice that is coamplified with Ki-ras (OMIM Ref. No. 190070) in the Y1 murine adrenal carcinoma cell line. The gene, designated Krag (Kirsten ras-associated gene) by them, consists of 3 exons and spans about 20 kb of genomic DNA. The Krag gene has a CG-rich promoter and first exon. The predicted 216-amino acid polypeptide encodes a protein with 4 potential hydrophobic domains, and its hydropathy plot resembles certain of the transmembrane-4 superfamily members such as CO-029 (OMIM Ref. No. 600769) and ME491 (OMIM Ref. No. 155740). An apparently homologous EST was mapped to chromosome 12. Heighway et al. (1996) isolated the hu-

man KRAG gene and showed that the predicted amino acid sequence is 91% identical to the mouse sequence. The human gene also contains 3 exons. Northern blots showed that KRAG is expressed in a variety of tissues with highest levels in muscle, where alternative splice variants were also observed. A YAC clone containing KRAG was mapped by fluorescence in situ hybridization to 12p11.2. One end of the YAC contained a sequence that was identical to that reported for inositol 1,4,5-triphosphate receptor type 2 (ITPR2; 600144), which had previously been mapped to 12p11. Heighway et al. (1996) showed that in certain tumors KRAS2, KRAG, and ITPR2 were all coamplified.

[36901] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36902] Heighway, J.; Betticher, D. C.; Hoban, P. R.; Altermatt, H. J.; Cowen, R. : Coamplification in tumors of KRAS2, type 2 inositol 1,4,5 triphosphate receptor gene, and a novel human gene, KRAG. Genomics 35: 207-214, 1996. ; and

[36903] Scott, A. F.; Elizaga, A.; Morrell, J.; Bergen, A.; Penno, M. B. : Characterization of a gene coamplified with Ki-ras in Y1 murine adrenal carcinoma cells that codes for a putative

memb.

[36904] Further studies establishing the function and utilities of SSPN are found in John Hopkins OMIM database record ID 601599, and in cited publications numbered 642 and 9335–9336 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM_003392) is another VGAM996 host target gene. WNT5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WNT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT5A BINDING SITE, designated SEQ ID:9428, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36905] Another function of VGAM996 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM_003392), a gene which is a ligand for members of the frizzled family of seven transmembrane receptors and is probably a developmental protein. Accordingly, utilities of VGAM996 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with WNT5A. The function of WNT5A has been established by previous studies. The Wnt genes belong to a family of protooncogenes with at least 13 known members that are expressed in species ranging from *Drosophila* to man. The name Wnt denotes the relationship of this family to the *Drosophila* segment polarity gene 'wingless' and to its vertebrate ortholog, *Int1*, a mouse protooncogene (see OMIM Ref. No. 164820). Transcription of Wnt family genes appears to be developmentally regulated in a precise temporal and spatial manner. The Wnt family is considered to be 1 of the 3 major families of signaling molecules in the mouse, the others being the fibroblast growth factor-related family (see OMIM Ref. No. 164980) and the transforming growth factor-beta-related family (TGFB; 190180). Using degenerate PCR and cDNA library screening to search for mouse genes related to Wnt1, Gavin et al. (1990) identified 6 new members of the Wnt gene family, including Wnt5a. The Wnt genes encode 38- to 43-kD cysteine-rich putative glycoproteins, which have features typical of secreted growth factors: a hydrophobic signal sequence and 21 conserved cysteine residues whose relative spacing is maintained.

Northern blot analysis detected expression of Wnt5a in brain, lung, and heart. At least 5 distinct Wnt5a transcripts were observed, which Gavin et al. (1990) hypothesized were due to transcript variability 5-prime to the initiation methionine. In situ hybridization detected a complex spatial and temporal pattern of Wnt5a in the mouse, including expression in the developing central nervous system, limbs, facial processes, and the posterior region of the fetus. Clark et al. (1993) cloned and sequenced several overlapping cDNAs encoding approximately 4.1 kb of the human homolog of Wnt5A. Expression of the human gene, symbolized WNT5A, was detected only in neonatal heart and lung. He et al. (1997) showed that human frizzled-5 (OMIM Ref. No. 601723) is the receptor for the Wnt5A ligand.

[36906] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36907] Gavin, B. J.; McMahon, J. A.; McMahon, A. P. : Expression of multiple novel Wnt-1/int-1-related genes during fetal and adult mouse development. Genes Dev. 4: 2319-2332, 1990. ; and

[36908] He, X.; Saint-Jeannet, J.-P.; Wang, Y.; Nathans, J.; Dawid,

I.; Varmus, H. : A member of the frizzled protein family mediating axis induction by Wnt-5A. Science 275: 1652-1654, 1997.

[36909] Further studies establishing the function and utilities of WNT5A are found in John Hopkins OMIM database record ID 164975, and in cited publications numbered 328 and 12747 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDT6 (Accession NM_021146) is another VGAM996 host target gene. CDT6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDT6 BINDING SITE, designated SEQ ID:22118, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36910] Another function of VGAM996 is therefore inhibition of CDT6 (Accession NM_021146). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDT6. FLJ23251 (Accession NM_024818) is another VGAM996 host target gene. FLJ23251 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ23251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23251 BINDING SITE, designated SEQ ID:24209, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36911] Another function of VGAM996 is therefore inhibition of FLJ23251 (Accession NM_024818). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23251. KIAA0461 (Accession XM_047883) is another VGAM996 host target gene. KIAA0461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0461 BINDING SITE, designated SEQ ID:35073, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36912] Another function of VGAM996 is therefore inhibition of

KIAA0461 (Accession XM_047883). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0461. KIAA1819 (Accession XM_045716) is another VGAM996 host target gene. KIAA1819 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1819 BINDING SITE, designated SEQ ID:34532, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36913] Another function of VGAM996 is therefore inhibition of KIAA1819 (Accession XM_045716). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1819. MAC30 (Accession XM_031536) is another VGAM996 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAC30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ ID:31402, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36914] Another function of VGAM996 is therefore inhibition of MAC30 (Accession XM_031536). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6A (SEMA6A, Accession NM_020796) is another VGAM996 host target gene. SEMA6A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA6A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA6A BINDING SITE, designated SEQ ID:21879, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36915] Another function of VGAM996 is therefore inhibition of Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6A (SEMA6A, Accession

NM_020796). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA6A. Tumor Protein D52 (TPD52, Accession NM_005079) is another VGAM996 host target gene. TPD52 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TPD52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPD52 BINDING SITE, designated SEQ ID:11530, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36916] Another function of VGAM996 is therefore inhibition of Tumor Protein D52 (TPD52, Accession NM_005079). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPD52. LOC124460 (Accession XM_071892) is another VGAM996 host target gene. LOC124460 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC124460 BINDING SITE, designated SEQ ID:37441, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36917] Another function of VGAM996 is therefore inhibition of LOC124460 (Accession XM_071892). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124460. LOC130814 (Accession XM_059471) is another VGAM996 host target gene. LOC130814 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130814 BINDING SITE, designated SEQ ID:37007, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36918] Another function of VGAM996 is therefore inhibition of LOC130814 (Accession XM_059471). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130814. LOC131827 (Accession XM_059536) is an-

other VGAM996 host target gene. LOC131827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131827 BINDING SITE, designated SEQ ID:37013, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36919] Another function of VGAM996 is therefore inhibition of LOC131827 (Accession XM_059536). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131827. LOC136319 (Accession XM_059839) is another VGAM996 host target gene. LOC136319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC136319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC136319 BINDING SITE, designated SEQ ID:37101, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36920] Another function of VGAM996 is therefore inhibition of LOC136319 (Accession XM_059839). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC136319. LOC148267 (Accession XM_086129) is another VGAM996 host target gene. LOC148267 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148267 BINDING SITE, designated SEQ ID:38516, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36921] Another function of VGAM996 is therefore inhibition of LOC148267 (Accession XM_086129). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148267. LOC221806 (Accession XM_166518) is another VGAM996 host target gene. LOC221806 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221806, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221806 BINDING SITE, designated SEQ ID:44453, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36922] Another function of VGAM996 is therefore inhibition of LOC221806 (Accession XM_166518). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221806. LOC91445 (Accession XM_018516) is another VGAM996 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30366, to the nucleotide sequence of VGAM996 RNA, herein designated VGAM RNA, also designated SEQ ID:3707.

[36923] Another function of VGAM996 is therefore inhibition of LOC91445 (Accession XM_018516). Accordingly, utilities of VGAM996 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91445. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 997 (VGAM997) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36924] VGAM997 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM997 was detected is described hereinabove with reference to Figs. 1–8.

[36925] VGAM997 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36926] VGAM997 gene encodes a VGAM997 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM997 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM997 precursor RNA is designated SEQ ID:983, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:983 is located at position 65867 relative to the genome of Cowpox Virus.

[36927] VGAM997 precursor RNA folds onto itself, forming VGAM997 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36928] An enzyme complex designated DICER COMPLEX, `dices` the VGAM997 folded precursor RNA into VGAM997 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM997 RNA is designated SEQ ID:3708, and is provided hereinbelow with reference to the sequence listing part.

[36929] VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM997 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36930] VGAM997 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM997 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM997 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36931] The complementary binding of VGAM997 RNA, herein designated VGAM RNA, to host target binding sites on VGAM997 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM997 host target RNA into VGAM997 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36932] It is appreciated that VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM997 host target genes. The mRNA of each one of this plurality of VGAM997 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM997 RNA, herein designated VGAM RNA, and which when bound by VGAM997 RNA causes in-

hibition of translation of respective one or more VGAM997 host target proteins.

[36933] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM997 gene, herein designated VGAM GENE, on one or more VGAM997 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36934] It is yet further appreciated that a function of VGAM997 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM997 include diagnosis, prevention and

treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM997 correlate with, and may be deduced from, the identity of the host target genes which VGAM997 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [36935] Nucleotide sequences of the VGAM997 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM997 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM997 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM997 are further described hereinbelow with reference to Table 1.
- [36936] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM997 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM997 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [36937] As mentioned hereinabove with reference to Fig. 1, a function of VGAM997 gene, herein designated VGAM is inhibition of expression of VGAM997 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM997 correlate with, and may be deduced from, the identity of the target genes which VGAM997 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36938] Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM_000838) is a VGAM997 host target gene. GRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM1 BINDING SITE, designated SEQ ID:6494, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36939] A function of VGAM997 is therefore inhibition of Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM_000838), a gene which promotes phosphoinositide hydrolysis. Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM1. The function of GRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM786. Solute Carrier Family 13 (sodium/sulfate symporters), Member 1 (SLC13A1, Accession NM_022444) is another VGAM997 host target gene. SLC13A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC13A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC13A1 BINDING SITE, designated SEQ ID:22774, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36940] Another function of VGAM997 is therefore inhibition of Solute Carrier Family 13 (sodium/sulfate symporters), Member 1 (SLC13A1, Accession NM_022444). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC13A1. GFR (Accession NM_012294) is another VGAM997 host target gene. GFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14636, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36941] Another function of VGAM997 is therefore inhibition of GFR (Accession NM_012294). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. KIAA1878 (Accession XM_166256) is another VGAM997 host target gene. KIAA1878 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1878 BINDING SITE, designated SEQ ID:44074, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36942] Another function of VGAM997 is therefore inhibition of KIAA1878 (Accession XM_166256). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1878. LOC222681 (Accession XM_167116) is another

VGAM997 host target gene. LOC222681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222681 BINDING SITE, designated SEQ ID:44614, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36943] Another function of VGAM997 is therefore inhibition of LOC222681 (Accession XM_167116). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222681. LOC257507 (Accession XM_175204) is another VGAM997 host target gene. LOC257507 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257507 BINDING SITE, designated SEQ ID:46680, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36944] Another function of VGAM997 is therefore inhibition of LOC257507 (Accession XM_175204). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257507. LOC257625 (Accession XM_175267) is another VGAM997 host target gene. LOC257625 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257625 BINDING SITE, designated SEQ ID:46736, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36945] Another function of VGAM997 is therefore inhibition of LOC257625 (Accession XM_175267). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257625. LOC93297 (Accession XM_050370) is another VGAM997 host target gene. LOC93297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93297, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93297 BINDING SITE, designated SEQ ID:35615, to the nucleotide sequence of VGAM997 RNA, herein designated VGAM RNA, also designated SEQ ID:3708.

[36946] Another function of VGAM997 is therefore inhibition of LOC93297 (Accession XM_050370). Accordingly, utilities of VGAM997 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93297. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 998 (VGAM998) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36947] VGAM998 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM998 was detected is described hereinabove with reference to Figs. 1–8.

[36948] VGAM998 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM998 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[36949] VGAM998 gene encodes a VGAM998 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM998 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM998 precursor RNA is designated SEQ ID:984, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:984 is located at position 64470 relative to the genome of Cowpox Virus.

[36950] VGAM998 precursor RNA folds onto itself, forming VGAM998 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36951] An enzyme complex designated DICER COMPLEX, `dices` the VGAM998 folded precursor RNA into VGAM998 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM998 RNA is designated SEQ ID:3709, and is provided hereinbelow with reference to the sequence listing part.

[36952] VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM998 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36953] VGAM998 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM998 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM998 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36954] The complementary binding of VGAM998 RNA, herein designated VGAM RNA, to host target binding sites on VGAM998 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM998 host target RNA into VGAM998 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[36955] It is appreciated that VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM998 host target genes. The mRNA of each one of this plurality of VGAM998 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM998 RNA, herein designated VGAM RNA, and which when bound by VGAM998 RNA causes inhibition of translation of respective one or more VGAM998 host target proteins.

[36956] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM998 gene, herein designated VGAM GENE, on one or more VGAM998 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36957] It is yet further appreciated that a function of VGAM998 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM998 correlate with, and may be deduced from, the identity of the host target genes which VGAM998 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36958] Nucleotide sequences of the VGAM998 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM998 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM998 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM998 are further described hereinbelow with reference to Table 1.

[36959] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM998 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM998 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36960] As mentioned hereinabove with reference to Fig. 1, a function of VGAM998 gene, herein designated VGAM is inhibition of expression of VGAM998 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM998 correlate with, and may be deduced from, the identity of the target genes which VGAM998 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36961] Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM_006693) is a VGAM998 host target gene. CPSF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPSF4 BINDING SITE, designated SEQ ID:13511, to the nucleotide sequence of VGAM998 RNA,

herein designated VGAM RNA, also designated SEQ ID:3709.

[36962] A function of VGAM998 is therefore inhibition of Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM_006693), a gene which may bind DNA. Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPSF4. The function of CPSF4 has been established by previous studies. Nemeroff et al. (1998) used the yeast 2-hybrid interaction trap to screen a human HeLa cDNA library for proteins that interact with the effector domain of the influenza A virus NS1 protein. They identified 1 such protein, termed NEB1 (NS1 effector domain-binding protein-1), which was almost identical to the bovine cleavage-polyadenylation specificity factor (CPSF) 30-kD subunit (Barabino et al., 1997). The human CPSF30 protein contains 236 amino acids. CPSF30 is an essential component of the 3-prime end processing machinery of cellular pre-mRNAs. In influenza virus-infected cells, the NS1 protein is physically associated with CPSF30. Binding of the NS1 protein to the CPSF30 protein in vitro prevents CPSF binding to the RNA substrate and inhibits 3-prime end cleavage and polyadenylation of host

pre-mRNAs. The NS1 protein also inhibits 3-prime end processing in vivo, and the uncleaved pre-mRNA remains in the nucleus. Via this regulation of pre-mRNA 3-prime end processing, the NS1 protein selectively inhibits the nuclear export of cellular, and not viral, mRNAs.

[36963] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[36964] Nemeroff, M. E.; Barabino, S. M. L.; Li, Y.; Keller, W.; Krug, R. M. : Influenza virus NS1 protein interacts with the cellular 30 kDa subunit of CPSF and inhibits 3-prime end formation of cellular pre-mRNAs. *Molec. Cell* 1: 991-1000, 1998. ; and

[36965] Barabino, S. M. L.; Hubner, W.; Jenny, A.; Minvielle-Sebastia, L.; Keller, W. : The 30 kDa subunit of mammalian cleavage and polyadenylation specificity factor and its yeast homolog are.

[36966] Further studies establishing the function and utilities of CPSF4 are found in John Hopkins OMIM database record ID 603052, and in cited publications numbered 8015-8016 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Von Hippel-Lindau Syndrome (VHL, Accession NM_000551) is another

VGAM998 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6163, to the nucleotide sequence of VGAM998 RNA, herein designated VGAM RNA, also designated SEQ ID:3709.

[36967] Another function of VGAM998 is therefore inhibition of Von Hippel-Lindau Syndrome (VHL, Accession NM_000551), a gene which may control rna stability through the selective degradation of rna-bound proteins. Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM197.IMPACT (Accession NM_018439) is another VGAM998 host target gene. IMPACT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPACT, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPACT BINDING SITE, designated SEQ ID:20505, to the nucleotide sequence of VGAM998 RNA, herein designated VGAM RNA, also designated SEQ ID:3709.

[36968] Another function of VGAM998 is therefore inhibition of IMPACT (Accession NM_018439). Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPACT. MGC20496 (Accession NM_052845) is another VGAM998 host target gene. MGC20496 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20496 BINDING SITE, designated SEQ ID:27425, to the nucleotide sequence of VGAM998 RNA, herein designated VGAM RNA, also designated SEQ ID:3709.

[36969] Another function of VGAM998 is therefore inhibition of MGC20496 (Accession NM_052845). Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC20496. Triple Homeobox 1 (TIX1, Accession XM_029734) is another VGAM998 host target gene. TIX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIX1 BINDING SITE, designated SEQ ID:30930, to the nucleotide sequence of VGAM998 RNA, herein designated VGAM RNA, also designated SEQ ID:3709.

[36970] Another function of VGAM998 is therefore inhibition of Triple Homeobox 1 (TIX1, Accession XM_029734). Accordingly, utilities of VGAM998 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIX1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 999 (VGAM999) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36971] VGAM999 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM999 was detected is described hereinabove with reference to Figs. 1–8.

[36972] VGAM999 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36973] VGAM999 gene encodes a VGAM999 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM999 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM999 precursor RNA is designated SEQ ID:985, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:985 is located at position 62693 relative to the genome of Cowpox Virus.

[36974] VGAM999 precursor RNA folds onto itself, forming VGAM999 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36975] An enzyme complex designated DICER COMPLEX, `dices` the VGAM999 folded precursor RNA into VGAM999 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 69%) nucleotide sequence of VGAM999 RNA is designated SEQ ID:3710, and is provided hereinbelow with reference to the sequence listing part.

[36976] VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM999 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36977] VGAM999 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM999 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM999 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[36978] The complementary binding of VGAM999 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM999 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM999 host target RNA into VGAM999 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36979] It is appreciated that VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM999 host target genes. The mRNA of each one of this plurality of VGAM999 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM999 RNA, herein designated VGAM RNA, and which when bound by VGAM999 RNA causes inhibition of translation of respective one or more VGAM999 host target proteins.

[36980] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM999 gene, herein designated VGAM GENE, on one or more VGAM999 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36981] It is yet further appreciated that a function of VGAM999 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM999 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM999 correlate with, and may be deduced from, the identity of the host target genes which VGAM999 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[36982] Nucleotide sequences of the VGAM999 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM999 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM999 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM999 are further described hereinbelow with reference to Table 1.

[36983] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM999 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM999 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[36984] As mentioned hereinabove with reference to Fig. 1, a function of VGAM999 gene, herein designated VGAM is inhibition of expression of VGAM999 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM999 correlate with, and may be deduced from, the identity of the target genes which VGAM999 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[36985] Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is a VGAM999 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14877, to the nucleotide sequence of VGAM999 RNA, herein designated VGAM RNA, also designated SEQ ID:3710.

[36986] A function of VGAM999 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM999 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.KIAA1468 (Accession XM_166289) is another VGAM999 host target gene. KIAA1468 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of KIAA1468 BINDING SITE, designated SEQ ID:44097, to the nucleotide sequence of VGAM999 RNA, herein designated VGAM RNA, also designated SEQ ID:3710.

[36987] Another function of VGAM999 is therefore inhibition of KIAA1468 (Accession XM_166289). Accordingly, utilities of VGAM999 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1468. KIAA1979 (Accession XM_113984) is another VGAM999 host target gene. KIAA1979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1979 BINDING SITE, designated SEQ ID:42588, to the nucleotide sequence of VGAM999 RNA, herein designated VGAM RNA, also designated SEQ ID:3710.

[36988] Another function of VGAM999 is therefore inhibition of KIAA1979 (Accession XM_113984). Accordingly, utilities of VGAM999 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1979. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1000 (VGAM1000) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[36989] VGAM1000 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1000 was detected is described hereinabove with reference to Figs. 1–8.

[36990] VGAM1000 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[36991] VGAM1000 gene encodes a VGAM1000 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1000 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1000 precursor RNA is designated SEQ ID:986, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:986 is located at position 63271 relative to the genome of Cowpox Virus.

[36992] VGAM1000 precursor RNA folds onto itself, forming VGAM1000 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[36993] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1000 folded precursor RNA into VGAM1000 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1000 RNA is designated SEQ ID:3711, and is provided hereinbelow with reference to the sequence listing part.

[36994] VGAM1000 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1000 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[36995] VGAM1000 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1000 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1000 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1000 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[36996] The complementary binding of VGAM1000 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1000 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1000 host target RNA into VGAM1000 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[36997] It is appreciated that VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1000 host target genes. The mRNA of each one of this plurality of VGAM1000 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1000 RNA, herein designated VGAM RNA, and which when bound by VGAM1000 RNA causes inhibition of translation of respective one or more

VGAM1000 host target proteins.

[36998] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1000 gene, herein designated VGAM GENE, on one or more VGAM1000 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[36999] It is yet further appreciated that a function of VGAM1000 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific

functions, and accordingly utilities, of VGAM1000 correlate with, and may be deduced from, the identity of the host target genes which VGAM1000 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37000] Nucleotide sequences of the VGAM1000 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1000 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1000 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1000 are further described hereinbelow with reference to Table 1.

[37001] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1000 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1000 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37002] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1000 gene, herein designated VGAM is inhibition of expression of VGAM1000 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1000 correlate with, and may be deduced from, the identity of the target genes which VGAM1000 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37003] EphB1 (EPHB1, Accession NM_004441) is a VGAM1000 host target gene. EPHB1 BINDING SITE1 and EPHB1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EPHB1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB1 BINDING SITE1 and EPHB1 BINDING SITE2, designated SEQ ID:10727 and SEQ ID:10726 respectively, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37004] A function of VGAM1000 is therefore inhibition of EphB1 (EPHB1, Accession NM_004441), a gene which receptor for members of the ephrin-b family. binds to ephrin-b1, -b2 and -b3. Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB1. The function of EPHB1 has been established by previous studies. See 179610 for background on Eph receptors and their ligands, the

ephrins. Tang et al. (1995) cloned and characterized a member of the EPH-related receptor protein tyrosine kinases and designated it NET (neuronally expressed EPH-related tyrosine kinase). The cDNA was isolated from a fetal brain expression library using a monoclonal antibody. The 3.9-kb RNA encodes a predicted protein of 984 amino acids with 2 hydrophobic regions corresponding to possible signal peptide and transmembrane domains. The NET protein shares 99% amino acid identity with Elk, the rat homolog. Northern blots showed maximal NET expression in the nervous system and in some tumor cell lines derived from neuroectoderm. Using immunohistochemical analysis of the developing mouse hindbrain, Cowan et al. (2000) detected Ephb1 expression in the floor plate and in hindbrain regions where facial and inner ear efferent neurons are located. Contractor et al. (2002) reported that mossy fiber long-term potentiation was reduced by perfusion of postsynaptic neurons with peptides and antibodies that interfere with binding of EphB receptor tyrosine kinases to the PDZ protein GRIP (GRIP1; 604597). Mossy fiber long-term potentiation was also reduced by extracellular application of soluble forms of beta-ephrins, which are normally membrane-anchored

presynaptic ligands for the EphB receptors. The application of soluble ligands for presynaptic ephrins increased basal excitatory transmission and occluded both tetanus and forskolin-induced synaptic potentiation. Contractor et al. (2002) concluded that the PDZ interactions in postsynaptic neuron and transsynaptic interactions between postsynaptic EphB receptors and presynaptic beta-ephrins are necessary for the induction of mossy fiber long-term potentiation. Tang et al. (1995) mapped the EPHB1 gene to 3q21-q23 by fluorescence in situ hybridization.

[37005] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37006] Tang, X. X.; Biegel, J. A.; Nycum, L. M.; Yoshioka, A.; Brodeur, G. M.; Pleasure, D. E.; Ikegaki, N. : cDNA cloning, molecular characterization, and chromosomal localization of NET (EPHT2), a human EPH-related receptor protein-tyrosine kinase gene preferentially expressed in brain. :Genomics 29: 426-437, 1995. ; and

[37007] Contractor, A.; Rogers, C.; Maron, C.; Henkemeyer, M.; Swanson, G. T.; Heinemann, S. F. : Trans-synaptic Eph receptor-ephrin signaling in hippocampal mossy fiber LTP. Science 296: 1864-1.

[37008] Further studies establishing the function and utilities of EPHB1 are found in John Hopkins OMIM database record ID 600600, and in cited publications numbered 1038 and 12328 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. V-myc Myelocytomatosis Viral Oncogene Homolog 2 (avian) (MYCL2, Accession NM_005377) is another VGAM1000 host target gene. MYCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCL2 BINDING SITE, designated SEQ ID:11854, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37009] Another function of VGAM1000 is therefore inhibition of V-myc Myelocytomatosis Viral Oncogene Homolog 2 (avian) (MYCL2, Accession NM_005377). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCL2. Prokineticin 1 (PROK1, Accession NM_032414) is another VGAM1000 host target gene.

PROK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROK1 BINDING SITE, designated SEQ ID:26195, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37010] Another function of VGAM1000 is therefore inhibition of Prokineticin 1 (PROK1, Accession NM_032414), a gene which induces proliferation, migration and fenestration in capillary endothelial cells derived from endocrine glands. Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROK1. The function of PROK1 has been established by previous studies. Endocrine gland-derived vascular endothelial growth factor (EG-VEGF) induces proliferation, migration, and fenestration in capillary endothelial cells derived from endocrine glands. Its expression is induced by hypoxia and is restricted to the steroidogenic glands (ovary, testis, adrenal, and placenta). Its expression is often complementary to the expression

of VEGF (OMIM Ref. No. 192240), suggesting that these molecules function in a coordinated manner. LeCouter et al. (2001) screened a library of purified human secreted proteins for the ability to induce proliferation in primary bovine adrenal cortex–derived capillary endothelial cells. EG–VEGF was capable of inducing a strong and reproducible mitogenic response. Mature EG–VEGF is a protein with a relative molecular mass of 8,600 encoded by a cDNA cloned from human ovary library. The 1.4–kb cDNA encodes a protein of 105 amino acids with a well defined signal sequence. The mature protein is predicted to have 86 amino acids, including 10 cysteines, and an expected isoelectric point of 8.46. These cysteines potentially form 5 disulfide bridges. EG–VEGF displays a high degree of homology to a nontoxic protein purified from the venom of the black mamba snake, venom protein A (VPRA). The structure of native VPRA was solved, and the disulfide bridge partners were revealed. The number and spacing of cysteines are completely conserved between VPRA and EG–VEGF. BV8, a human molecule closely related to a peptide isolated from the yellow–bellied toad, is 58% identical to the EG–VEGF mature protein. There is also significant homology to the carboxy–terminal sequence of *Xenopus*

dickkopf (see OMIM Ref. No. 605189) and to colipase (OMIM Ref. No. 120105). Li et al. (2001) identified EG-VEGF as prokineticin-1. EG-VEGF is mitogenic and chemoattractive and able to induce fenestration. EG-VEGF expression is induced by hypoxia, and there is an HIF1 (OMIM Ref. No. 603348) binding site present on EG-VEGF. EG-VEGF is able to induce angiogenesis and ovarian cyst formation. Northern blot analysis demonstrated expression in testis, ovary, adrenal gland, and placenta. A signal was detectable in prostate after prolonged exposure

[37011] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37012] LeCouter, J.; Kowalski, J.; Foster, J.; Hass, P.; Zhang, Z.; Dillard-Telm, L.; Frantz, G.; Rangell, L.; DeGuzman, L.; Keller, G.-A.; Peale, F.; Gurney, P.; Hillan, K. J.; Ferrara, N. : Identification of an angiogenic mitogen selective for endocrine gland endothelium. Nature 412: 877-884, 2001. ; and

[37013] Li, M.; Bullock, C. M.; Knauer, D. J.; Ehlert, F. J.; Zhou, Q. Y. : Identification of two prokineticin cDNAs: recombinant proteins potently contract gastrointestinal smooth muscle. Mol.

[37014] Further studies establishing the function and utilities of PROK1 are found in John Hopkins OMIM database record ID 606233, and in cited publications numbered 6644–6645 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Titin Immunoglobulin Domain Protein (myotilin) (TTID, Accession NM_006790) is another VGAM1000 host target gene. TTID BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TTID, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTID BINDING SITE, designated SEQ ID:13668, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37015] Another function of VGAM1000 is therefore inhibition of Titin Immunoglobulin Domain Protein (myotilin) (TTID, Accession NM_006790), a gene which is a sarcomeric structural protein. Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTID. The function of TTID has been established by previous studies. By radiation hybrid mapping, Salmikangas et al. (1999) located the

myotilin gene on 5q31 between markers AFM350yB1 and D5S500. The locus of a dominantly inherited limb-girdle muscular dystrophy, LGMD1A (OMIM Ref. No. 159000), resides in an overlapping narrow segment, and a form of distal myopathy with vocal cord and pharyngeal weakness (OMIM Ref. No. 158580) maps to the same region. Muscle specificity and apparent role as a sarcomeric structural protein raise the possibility that defects in the myotilin gene may cause muscular dystrophy. Hauser et al. (2000) identified a mutation in the myotilin gene (thr57 to ile; 604103.0001) in a large North American family of German descent segregating LGMD1A. The mutant allele was transcribed, and normal levels of correctly localized myotilin protein were seen in LGMD1A muscle. The mutation did not disrupt binding to alpha-actinin.

[37016] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37017] Salmikangas, P.; Mykkanen, O.-M.; Gronholm, M.; Heiska, L.; Kere, J.; Carpen, O. : Myotilin, a novel sarcomeric protein with two Ig-like domains, is encoded by a candidate gene for limb-girdle muscular dystrophy. Hum. Molec. Genet. 8: 1329-1336, 1999. ; and

[37018] Hauser, M. A.; Horrigan, S. K.; Salmikangas, P.; Torian, U. M.; Viles, K. D.; Dancel, R.; Tim, R. W.; Taivainen, A.; Bartoloni, L.; Gilchrist, J. M.; Stajich, J. M.; Gaskell, P. C.; Gilber.

[37019] Further studies establishing the function and utilities of TTID are found in John Hopkins OMIM database record ID 604103, and in cited publications numbered 5084 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294) is another VGAM1000 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26062, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37020] Another function of VGAM1000 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294). Accordingly,

utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. DKFZp547I094 (Accession NM_032155) is another VGAM1000 host target gene. DKFZp547I094 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I094, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I094 BINDING SITE, designated SEQ ID:25854, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37021] Another function of VGAM1000 is therefore inhibition of DKFZp547I094 (Accession NM_032155). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I094. DKFZp761O17121 (Accession NM_032287) is another VGAM1000 host target gene. DKFZp761O17121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761O17121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761O17121 BINDING SITE, designated SEQ ID:26043, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37022] Another function of VGAM1000 is therefore inhibition of DKFZp761O17121 (Accession NM_032287). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761O17121. FLJ21438 (Accession XM_029084) is another VGAM1000 host target gene. FLJ21438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21438 BINDING SITE, designated SEQ ID:30842, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37023] Another function of VGAM1000 is therefore inhibition of FLJ21438 (Accession XM_029084). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ21438. Mab-21-like 2 (*C. elegans*) (MAB21L2, Accession NM_006439) is another VGAM1000 host target gene. MAB21L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAB21L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L2 BINDING SITE, designated SEQ ID:13147, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37024] Another function of VGAM1000 is therefore inhibition of Mab-21-like 2 (*C. elegans*) (MAB21L2, Accession NM_006439). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L2. MDN1, Midasin Homolog (yeast) (MDN1, Accession XM_031539) is another VGAM1000 host target gene. MDN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MDN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDN1 BIND-

ING SITE, designated SEQ ID:31408, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37025] Another function of VGAM1000 is therefore inhibition of MDN1, Midasin Homolog (yeast) (MDN1, Accession XM_031539). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDN1. LOC220766 (Accession XM_165471) is another VGAM1000 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43645, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37026] Another function of VGAM1000 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC255565 (Accession XM_170811) is an-

other VGAM1000 host target gene. LOC255565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255565 BINDING SITE, designated SEQ ID:45586, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37027] Another function of VGAM1000 is therefore inhibition of LOC255565 (Accession XM_170811). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255565. LOC92230 (Accession XM_043733) is another VGAM1000 host target gene. LOC92230 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92230 BINDING SITE, designated SEQ ID:34005, to the nucleotide sequence of VGAM1000 RNA, herein designated VGAM RNA, also designated SEQ ID:3711.

[37028] Another function of VGAM1000 is therefore inhibition of LOC92230 (Accession XM_043733). Accordingly, utilities of VGAM1000 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92230. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1001 (VGAM1001) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37029] VGAM1001 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1001 was detected is described hereinabove with reference to Figs. 1–8.

[37030] VGAM1001 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37031] VGAM1001 gene encodes a VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1001 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1001 precursor RNA is designated SEQ ID:987, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:987 is located at position 62554 relative to the genome of Cowpox Virus.

[37032] VGAM1001 precursor RNA folds onto itself, forming VGAM1001 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37033] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1001 folded precursor RNA into VGAM1001 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1001 RNA is designated SEQ ID:3712, and is provided hereinbelow with reference to the sequence listing part.

[37034] VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1001 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[37035] VGAM1001 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1001 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1001 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37036] The complementary binding of VGAM1001 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1001 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1001 host target RNA into VGAM1001 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37037] It is appreciated that VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1001 host target genes. The mRNA of each one of this plurality of VGAM1001 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1001 RNA, herein designated VGAM RNA, and which when bound by VGAM1001 RNA causes inhibition of translation of respective one or more VGAM1001 host target proteins.

[37038] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1001 gene, herein designated VGAM GENE, on one or more VGAM1001 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37039] It is yet further appreciated that a function of VGAM1001 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1001 correlate with, and may be deduced from, the identity of the host target genes which VGAM1001 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37040] Nucleotide sequences of the VGAM1001 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1001 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1001 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1001 are further described hereinbelow with reference to Table 1.

[37041] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1001 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1001 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[37042] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1001 gene, herein designated VGAM is inhibition of expression of VGAM1001 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1001 correlate with, and may be deduced from, the identity of the target genes which VGAM1001 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37043] Leucine Zipper-EF-hand Containing Transmembrane Protein 1 (LETM1, Accession NM_012318) is a VGAM1001 host target gene. LETM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LETM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LETM1 BINDING SITE, designated SEQ ID:14696, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37044] A function of VGAM1001 is therefore inhibition of Leucine Zipper-EF-hand Containing Transmembrane Protein 1 (LETM1, Accession NM_012318). Accordingly, utilities of

VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LETM1. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030667) is another VGAM1001 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ ID:25002, SEQ ID:25008, SEQ ID:25017, SEQ ID:25026 and SEQ ID:8737 respectively, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37045] Another function of VGAM1001 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030667), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM140.Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM1001 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15355, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37046] Another function of VGAM1001 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.ATP-binding Cassette, Sub-family C

(CFTR/MRP), Member 13 (ABCC13, Accession NM_138726) is another VGAM1001 host target gene. ABCC13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ABCC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC13 BINDING SITE, designated SEQ ID:28973, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37047] Another function of VGAM1001 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC13. Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM_025225) is another VGAM1001 host target gene. C22orf20 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C22orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf20 BINDING SITE,

designated SEQ ID:24901, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37048] Another function of VGAM1001 is therefore inhibition of Chromosome 22 Open Reading Frame 20 (C22orf20, Accession NM_025225). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf20.

FLJ12056 (Accession NM_024933) is another VGAM1001 host target gene. FLJ12056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12056 BINDING SITE, designated SEQ ID:24469, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37049] Another function of VGAM1001 is therefore inhibition of FLJ12056 (Accession NM_024933). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12056. FLJ20232 (Accession NM_019008) is another

VGAM1001 host target gene. FLJ20232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20232 BINDING SITE, designated SEQ ID:21085, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37050] Another function of VGAM1001 is therefore inhibition of FLJ20232 (Accession NM_019008). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20232. FLJ30681 (Accession XM_166291) is another VGAM1001 host target gene. FLJ30681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30681 BINDING SITE, designated SEQ ID:44105, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37051] Another function of VGAM1001 is therefore inhibition of FLJ30681 (Accession XM_166291). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30681. HSA249128 (Accession NM_017583) is another VGAM1001 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19028, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37052] Another function of VGAM1001 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA249128. KIAA0774 (Accession XM_166270) is another VGAM1001 host target gene. KIAA0774 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0774, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0774 BINDING SITE, designated SEQ ID:44087, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37053] Another function of VGAM1001 is therefore inhibition of KIAA0774 (Accession XM_166270). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0774. KIAA1164 (Accession XM_045358) is another VGAM1001 host target gene. KIAA1164 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1164 BINDING SITE, designated SEQ ID:34441, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37054] Another function of VGAM1001 is therefore inhibition of KIAA1164 (Accession XM_045358). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1164. KIAA1867 (Accession XM_170675) is another VGAM1001 host target gene. KIAA1867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1867 BINDING SITE, designated SEQ ID:45456, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37055] Another function of VGAM1001 is therefore inhibition of KIAA1867 (Accession XM_170675). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1867. LAP1B (Accession XM_035429) is another VGAM1001 host target gene. LAP1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAP1B BINDING SITE, designated SEQ ID:32264, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3712.

[37056] Another function of VGAM1001 is therefore inhibition of LAP1B (Accession XM_035429). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAP1B. MGC4796 (Accession XM_029031) is another VGAM1001 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30827, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37057] Another function of VGAM1001 is therefore inhibition of MGC4796 (Accession XM_029031). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. LOC134285 (Accession XM_072365) is another VGAM1001 host target gene. LOC134285 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC134285, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134285 BINDING SITE, designated SEQ ID:37490, to the nucleotide sequence of VGAM1001 RNA, herein designated VGAM RNA, also designated SEQ ID:3712.

[37058] Another function of VGAM1001 is therefore inhibition of LOC134285 (Accession XM_072365). Accordingly, utilities of VGAM1001 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134285. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1002 (VGAM1002) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37059] VGAM1002 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1002 was detected is described hereinabove with reference to Figs. 1-8.

[37060] VGAM1002 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cy-

tomegalovirus. VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37061] VGAM1002 gene encodes a VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1002 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1002 precursor RNA is designated SEQ ID:988, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:988 is located at position 198161 relative to the genome of Chimpanzee Cytomegalovirus.

[37062] VGAM1002 precursor RNA folds onto itself, forming VGAM1002 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37063] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1002 folded precursor RNA into VGAM1002 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1002 RNA is designated SEQ ID:3713, and is provided hereinbelow with reference to the sequence listing part.

[37064] VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1002 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37065] VGAM1002 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1002 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1002 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37066] The complementary binding of VGAM1002 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1002 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1002 host target RNA into VGAM1002 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37067] It is appreciated that VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1002 host target genes. The mRNA of each one of this plurality of VGAM1002 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1002 RNA, herein designated VGAM RNA, and which when bound by VGAM1002 RNA causes inhibition of translation of respective one or more VGAM1002 host target proteins.

[37068] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1002 gene, herein designated VGAM GENE, on one or more VGAM1002 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37069] It is yet further appreciated that a function of VGAM1002 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1002 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1002 correlate with, and may be deduced from, the identity of the host target genes which VGAM1002 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37070] Nucleotide sequences of the VGAM1002 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1002 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1002 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1002 are further described hereinbelow with reference to Table 1.

[37071] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1002 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1002 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37072] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1002 gene, herein designated VGAM is inhibition of expression of VGAM1002 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1002 correlate with, and may be deduced from, the identity of the target genes which VGAM1002 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37073] EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883) is a VGAM1002 host target gene. EGFL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30967, to the

nucleotide sequence of VGAM1002 RNA, herein designated VGAM RNA, also designated SEQ ID:3713.

[37074] A function of VGAM1002 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883). Accordingly, utilities of VGAM1002 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL4. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1003 (VGAM1003) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37075] VGAM1003 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1003 was detected is described hereinabove with reference to Figs. 1-8.

[37076] VGAM1003 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37077] VGAM1003 gene encodes a VGAM1003 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1003 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1003 precursor RNA is designated SEQ ID:989, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:989 is located at position 199498 relative to the genome of Chimpanzee Cytomegalovirus.

[37078] VGAM1003 precursor RNA folds onto itself, forming VGAM1003 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37079] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1003 folded precursor RNA into VGAM1003 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1003 RNA is designated SEQ ID:3714, and is provided hereinbelow with reference to the sequence listing part.

[37080] VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1003 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37081] VGAM1003 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1003 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1003 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37082] The complementary binding of VGAM1003 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1003 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1003 host target RNA into VGAM1003 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37083] It is appreciated that VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1003 host target genes. The mRNA of each one of this plurality of VGAM1003 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1003 RNA, herein designated VGAM RNA, and which when bound by VGAM1003 RNA causes inhibition of translation of respective one or more VGAM1003 host target proteins.

[37084] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1003 gene, herein designated VGAM GENE, on one or more VGAM1003 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[37085] It is yet further appreciated that a function of VGAM1003 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cy-tomegalovirus. Specific functions, and accordingly utilities, of VGAM1003 correlate with, and may be deduced from, the identity of the host target genes which VGAM1003 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37086] Nucleotide sequences of the VGAM1003 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1003 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1003 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1003 are further described hereinbelow with reference to Table 1.

[37087] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1003 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1003 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37088] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1003 gene, herein designated VGAM is inhibition of expression of VGAM1003 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1003 correlate with, and may be deduced from, the identity of the target genes which VGAM1003 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37089] DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Accession NM_001356) is a VGAM1003 host target gene. DDX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX3 BINDING SITE, designated SEQ ID:7033, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37090] A function of VGAM1003 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Ac-

cession NM_001356), a gene which interacts with hepatitis c virus core protein resulting a change in intracellular location. Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX3. The function of DDX3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM232.Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM_000838) is another VGAM1003 host target gene. GRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM1 BINDING SITE, designated SEQ ID:6495, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37091] Another function of VGAM1003 is therefore inhibition of Glutamate Receptor, Metabotropic 1 (GRM1, Accession NM_000838), a gene which promotes phosphoinositide hydrolysis. Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with GRM1. The function of GRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM786. Transient Receptor Potential Cation Channel, Subfamily V, Member 3 (TRPV3, Accession XM_170821) is another VGAM1003 host target gene. TRPV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV3 BINDING SITE, designated SEQ ID:45597, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37092] Another function of VGAM1003 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V, Member 3 (TRPV3, Accession XM_170821). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV3. FLJ10936 (Accession NM_018279) is another VGAM1003 host target gene. FLJ10936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ10936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10936 BINDING SITE, designated SEQ ID:20268, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37093] Another function of VGAM1003 is therefore inhibition of FLJ10936 (Accession NM_018279). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10936. phorbolin-1 (Accession XM_114206) is another VGAM1003 host target gene. phorbolin-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by phorbolin-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of phorbolin-1 BINDING SITE, designated SEQ ID:42798, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37094] Another function of VGAM1003 is therefore inhibition of phorbolin-1 (Accession XM_114206). Accordingly, utilities

of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with phorbolin-1. LOC151568 (Accession NM_138483) is another VGAM1003 host target gene. LOC151568 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151568 BINDING SITE, designated SEQ ID:28836, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37095] Another function of VGAM1003 is therefore inhibition of LOC151568 (Accession NM_138483). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151568. LOC151996 (Accession XM_098151) is another VGAM1003 host target gene. LOC151996 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC151996 BINDING SITE, designated SEQ ID:41413, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37096] Another function of VGAM1003 is therefore inhibition of LOC151996 (Accession XM_098151). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151996. LOC196759 (Accession XM_113601) is another VGAM1003 host target gene. LOC196759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196759 BINDING SITE, designated SEQ ID:42294, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37097] Another function of VGAM1003 is therefore inhibition of LOC196759 (Accession XM_113601). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196759. LOC201617 (Accession XM_117315) is another VGAM1003 host target gene. LOC201617 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201617 BINDING SITE, designated SEQ ID:43382, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37098] Another function of VGAM1003 is therefore inhibition of LOC201617 (Accession XM_117315). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201617. LOC220045 (Accession XM_167820) is another VGAM1003 host target gene. LOC220045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220045 BINDING SITE, designated SEQ ID:44859, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37099] Another function of VGAM1003 is therefore inhibition of

LOC220045 (Accession XM_167820). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220045. LOC93070 (Accession XM_049046) is another VGAM1003 host target gene. LOC93070 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93070 BINDING SITE, designated SEQ ID:35323, to the nucleotide sequence of VGAM1003 RNA, herein designated VGAM RNA, also designated SEQ ID:3714.

[37100] Another function of VGAM1003 is therefore inhibition of LOC93070 (Accession XM_049046). Accordingly, utilities of VGAM1003 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93070. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1004 (VGAM1004) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[37101] VGAM1004 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1004 was detected is described hereinabove with reference to Figs. 1–8.

[37102] VGAM1004 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37103] VGAM1004 gene encodes a VGAM1004 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1004 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1004 precursor RNA is designated SEQ ID:990, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:990 is located at position 199410 relative to the genome of Chimpanzee Cytomegalovirus.

[37104] VGAM1004 precursor RNA folds onto itself, forming VGAM1004 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37105] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1004 folded precursor RNA into VGAM1004 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1004 RNA is designated SEQ ID:3715, and is provided hereinbelow with reference to the sequence listing part.

[37106] VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1004 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[37107] VGAM1004 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1004 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1004 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[37108] The complementary binding of VGAM1004 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1004 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1004 host target RNA into VGAM1004 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37109] It is appreciated that VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1004 host target genes. The mRNA of each one of this plurality of VGAM1004 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1004 RNA, herein designated VGAM RNA, and which when bound by VGAM1004 RNA causes inhibition of translation of respective one or more VGAM1004 host target proteins.

[37110] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1004 gene, herein designated VGAM GENE, on one

or more VGAM1004 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37111] It is yet further appreciated that a function of VGAM1004 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1004 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1004 correlate with, and may be deduced from, the identity of the host target genes which VGAM1004 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37112] Nucleotide sequences of the VGAM1004 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1004 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1004 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1004 are further described hereinbelow with reference to Table 1.

[37113] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1004 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1004 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37114] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1004 gene, herein designated VGAM is inhibition of expression of VGAM1004 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1004 correlate with, and may be deduced from, the identity of the target genes which VGAM1004 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37115] FLJ20330 (Accession NM_018988) is a VGAM1004 host

target gene. FLJ20330 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20330 BINDING SITE, designated SEQ ID:21059, to the nucleotide sequence of VGAM1004 RNA, herein designated VGAM RNA, also designated SEQ ID:3715.

[37116] A function of VGAM1004 is therefore inhibition of FLJ20330 (Accession NM_018988). Accordingly, utilities of VGAM1004 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20330. PRO0529 (Accession NM_014074) is another VGAM1004 host target gene. PRO0529 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO0529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0529 BINDING SITE, designated SEQ ID:15298, to the nucleotide sequence of VGAM1004 RNA, herein designated VGAM RNA, also designated SEQ ID:3715.

[37117] Another function of VGAM1004 is therefore inhibition of PRO0529 (Accession NM_014074). Accordingly, utilities of VGAM1004 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0529. LOC93206 (Accession XM_049838) is another VGAM1004 host target gene. LOC93206 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93206 BINDING SITE, designated SEQ ID:35517, to the nucleotide sequence of VGAM1004 RNA, herein designated VGAM RNA, also designated SEQ ID:3715.

[37118] Another function of VGAM1004 is therefore inhibition of LOC93206 (Accession XM_049838). Accordingly, utilities of VGAM1004 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93206. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1005 (VGAM1005) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[37119] VGAM1005 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1005 was detected is described hereinabove with reference to Figs. 1-8.

[37120] VGAM1005 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37121] VGAM1005 gene encodes a VGAM1005 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1005 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1005 precursor RNA is designated SEQ ID:991, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:991 is located at position 196285 relative to the genome of Chimpanzee Cytomegalovirus.

[37122] VGAM1005 precursor RNA folds onto itself, forming VGAM1005 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37123] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1005 folded precursor RNA into VGAM1005 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1005 RNA is designated SEQ ID:3716, and is provided hereinbelow with reference to the sequence listing part.

[37124] VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1005 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37125] VGAM1005 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1005 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1005 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[37126] The complementary binding of VGAM1005 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1005 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1005 host target RNA into VGAM1005 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37127] It is appreciated that VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1005 host target genes. The mRNA of each one of this plurality of VGAM1005 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1005 RNA, herein designated VGAM RNA, and which when bound by VGAM1005 RNA causes inhibition of translation of respective one or more VGAM1005 host target proteins.

[37128] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1005 gene, herein designated VGAM GENE, on one or more VGAM1005 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37129] It is yet further appreciated that a function of VGAM1005 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1005 correlate with, and may be deduced from, the identity of the host target genes which VGAM1005 binds and inhibits, and the function of these

host target genes, as elaborated hereinbelow.

[37130] Nucleotide sequences of the VGAM1005 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1005 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1005 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1005 are further described hereinbelow with reference to Table 1.

[37131] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1005 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1005 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37132] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1005 gene, herein designated VGAM is inhibition of expression of VGAM1005 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1005 correlate with, and may be deduced from, the identity of the target genes which VGAM1005 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37133] HLA-B Associated Transcript 4 (BAT4, Accession NM_033177) is a VGAM1005 host target gene. BAT4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BAT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAT4 BINDING SITE, designated SEQ ID:27040, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37134] A function of VGAM1005 is therefore inhibition of HLA-B Associated Transcript 4 (BAT4, Accession NM_033177). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAT4. Cyclin D2 (CCND2, Accession NM_001759) is another VGAM1005 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7514, to the nucleotide sequence of VGAM1005 RNA,

herein designated VGAM RNA, also designated SEQ ID:3716.

[37135] Another function of VGAM1005 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the G1/s (start) transition. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Cell Division Cycle 34 (CDC34, Accession NM_004359) is another VGAM1005 host target gene. CDC34 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDC34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC34 BINDING SITE, designated SEQ ID:10561, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37136] Another function of VGAM1005 is therefore inhibition of Cell Division Cycle 34 (CDC34, Accession NM_004359).

Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC34. Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is another VGAM1005 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10698, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37137] Another function of VGAM1005 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2,

Pfeiffer syndrome) (FGFR1, Accession NM_015850) is another VGAM1005 host target gene. FGFR1 BINDING SITE1 through FGFR1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR1 BINDING SITE1 through FGFR1 BINDING SITE5, designated SEQ ID:17977, SEQ ID:23361, SEQ ID:23371, SEQ ID:23376 and SEQ ID:6206 respectively, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37138] Another function of VGAM1005 is therefore inhibition of Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM_015850). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR1. Fucosyltransferase 8 (alpha (1,6) Fucosyltransferase) (FUT8, Accession NM_004480) is another VGAM1005 host target gene. FUT8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FUT8, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT8 BINDING SITE, designated SEQ ID:10795, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37139] Another function of VGAM1005 is therefore inhibition of Fucosyltransferase 8 (alpha (1,6) Fucosyltransferase) (FUT8, Accession NM_004480), a gene which transfers fucose to N-linked type complex glycopeptides from GDP-Fuc; functions in asparagine-linked glycoprotein oligosaccharide synthesis. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT8. The function of FUT8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Glycyl-tRNA Synthetase (GARS, Accession NM_002047) is another VGAM1005 host target gene. GARS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of GARS BINDING SITE, designated SEQ ID:7796, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37140] Another function of VGAM1005 is therefore inhibition of Glycyl-tRNA Synthetase (GARS, Accession NM_002047), a gene which functions in protein biosynthesis. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARS. The function of GARS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM113. Guanine Nucleotide Binding Protein-like 1 (GNL1, Accession XM_166361) is another VGAM1005 host target gene. GNL1 BINDING SITE1 and GNL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GNL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNL1 BINDING SITE1 and GNL1 BINDING SITE2, designated SEQ ID:44187 and SEQ ID:46716 respectively, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37141] Another function of VGAM1005 is therefore inhibition of Guanine Nucleotide Binding Protein-like 1 (GNL1, Accession XM_166361). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNL1. Hippocalcin-like 1 (HPCAL1, Accession NM_002149) is another VGAM1005 host target gene. HPCAL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HPCAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCAL1 BINDING SITE, designated SEQ ID:7928, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37142] Another function of VGAM1005 is therefore inhibition of Hippocalcin-like 1 (HPCAL1, Accession NM_002149). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL1. Iduronate 2-sulfatase (Hunter syndrome) (IDS, Accession NM_000202) is another VGAM1005 host target gene. IDS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by IDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDS BINDING SITE, designated SEQ ID:5697, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37143] Another function of VGAM1005 is therefore inhibition of Iduronate 2-sulfatase (Hunter syndrome) (IDS, Accession NM_000202). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDS. Jagged 2 (JAG2, Accession NM_002226) is another VGAM1005 host target gene. JAG2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by JAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAG2 BINDING SITE, designated SEQ ID:8005, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37144] Another function of VGAM1005 is therefore inhibition of Jagged 2 (JAG2, Accession NM_002226), a gene which is a

putative notch ligand involved in the mediation of notch signaling. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAG2. The function of JAG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM136. Met Proto-oncogene (hepatocyte growth factor receptor) (MET, Accession XM_048918) is another VGAM1005 host target gene. MET BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MET, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MET BINDING SITE, designated SEQ ID:35304, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37145] Another function of VGAM1005 is therefore inhibition of Met Proto-oncogene (hepatocyte growth factor receptor) (MET, Accession XM_048918), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with MET. The function of MET has been established by previous studies. In mammals, 5-prime-terminal caps are formed on nascent pre-mRNAs by the sequential action of 2 enzymes, the bifunctional capping enzyme RNGTT (OMIM Ref. No. 603512) and RNA (guanine-7) methyltransferase. RNGTT catalyzes the removal of the gamma-phosphate of the initiating nucleotide and transfers GMP from GTP to the resulting diphosphate end. RNA (guanine-7) methyltransferase catalyzes the subsequent N7 methylation of the newly formed termini. The terminal 7-methylguanosine is recognized by cap-binding proteins that facilitate key events in gene expression. By searching an EST database for sequences homologous to that of *S. cerevisiae* RNA (guanine-7) methyltransferase, Pillutla et al. (1998) identified a human Met cDNA. The predicted 476-amino acid MET protein contains several conserved motifs known to be required for methyltransferase activity. Recombinant Met exhibited RNA (guanine-7) methyltransferase activity in vitro, and formed ternary complexes with RNGTT and the elongating form of RNA polymerase II. By screening human brain cDNAs for those encoding large proteins, Ishikawa et al. (1997) identified KIAA0398, an RNMT cDNA. Tsukamoto et al. (1998) isolated 3 human

cDNAs encoding mRNA RNMT, which they termed HCMT1a, HCMT1b, and HCMT1c, which appear to be produced by alternative splicing. HCMT1a and HCMT1b encode deduced proteins of 476 and 504 amino acids, respectively, and differ only in the region encoding the C-terminal portion of the enzyme after residue 465. HCMT1c appears to encode the same polypeptide as HCMT1a; however, the 3-prime noncoding region of HCMT1c contains sequences corresponding to portions of both HCMT1a and HCMT1b. RT-PCR detected expression of the 3 mRNAs in all tissues tested. Recombinant HCMT1a expressed in *E. coli* exhibited mRNA RNMT activity, whereas recombinant HCMT1b did not. By analysis of a radiation hybrid panel, Pillutla et al. (1998) and Ishikawa et al. (1997) mapped the RNMT gene to chromosome 18. Pillutla et al. (1998) refined the location to 18p11.23–p11.22 using fluorescence in situ hybridization.

[37146] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37147] Pillutla, R. C.; Yue, Z.; Maldonado, E.; Shatkin, A. J. : Recombinant human mRNA cap methyltransferase binds

capping enzyme/RNA polymerase II complexes. J. Biol. Chem. 273: 21443–21446, 1998. ; and

[37148] Tsukamoto, T.; Shibagaki, Y.; Niikura, Y.; Mizumoto, K. : Cloning and characterization of three human cDNAs encoding mRNA (guanine-7)-methyltransferase, an mRNA cap methylase. Biochem. B.

[37149] Further studies establishing the function and utilities of MET are found in John Hopkins OMIM database record ID 603514, and in cited publications numbered 110 and 1110–1111 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neurexin 1 (NRXN1, Accession NM_138735) is another VGAM1005 host target gene. NRXN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRXN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN1 BINDING SITE, designated SEQ ID:28995, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37150] Another function of VGAM1005 is therefore inhibition of Neurexin 1 (NRXN1, Accession NM_138735), a gene which

may be involved in cell recognition, cell adhesion, and mediate intracellular signaling. Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN1. The function of NRXN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281) is another VGAM1005 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42837, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37151] Another function of VGAM1005 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A.

Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459) is another VGAM1005 host target gene. SLC30A3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC30A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC30A3 BINDING SITE, designated SEQ ID:9524, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37152] Another function of VGAM1005 is therefore inhibition of Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC30A3. Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916) is another VGAM1005 host target gene. AP1S2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AP1S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of AP1S2 BINDING SITE, designated SEQ ID:10002, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37153] Another function of VGAM1005 is therefore inhibition of Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1S2. Chromosome 22 Open Reading Frame 4 (C22orf4, Accession XM_027143) is another VGAM1005 host target gene. C22orf4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf4 BINDING SITE, designated SEQ ID:30424, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37154] Another function of VGAM1005 is therefore inhibition of Chromosome 22 Open Reading Frame 4 (C22orf4, Accession XM_027143). Accordingly, utilities of VGAM1005 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf4. CHFR (Accession NM_018223) is another VGAM1005 host target gene. CHFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHFR BINDING SITE, designated SEQ ID:20148, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37155] Another function of VGAM1005 is therefore inhibition of CHFR (Accession NM_018223). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHFR. DKFZp547C176 (Accession XM_040799) is another VGAM1005 host target gene. DKFZp547C176 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp547C176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547C176 BINDING SITE, designated SEQ

ID:33380, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37156] Another function of VGAM1005 is therefore inhibition of DKFZp547C176 (Accession XM_040799). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547C176. DKFZP564I1171 (Accession XM_049568) is another VGAM1005 host target gene. DKFZP564I1171 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564I1171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I1171 BINDING SITE, designated SEQ ID:35443, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37157] Another function of VGAM1005 is therefore inhibition of DKFZP564I1171 (Accession XM_049568). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I1171. DKFZp761A052 (Accession

XM_054098) is another VGAM1005 host target gene. DKFZp761A052 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761A052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761A052 BINDING SITE, designated SEQ ID:36141, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37158] Another function of VGAM1005 is therefore inhibition of DKFZp761A052 (Accession XM_054098). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761A052. FLJ13262 (Accession NM_024914) is another VGAM1005 host target gene. FLJ13262 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13262 BINDING SITE, designated SEQ ID:24433, to the nucleotide sequence of VGAM1005 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3716.

[37159] Another function of VGAM1005 is therefore inhibition of FLJ13262 (Accession NM_024914). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13262. FLJ20979 (Accession NM_024121) is another VGAM1005 host target gene. FLJ20979 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20979 BINDING SITE, designated SEQ ID:23574, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37160] Another function of VGAM1005 is therefore inhibition of FLJ20979 (Accession NM_024121). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20979. GABA(A) Receptors Associated Protein Like 3 (GABARAPL3, Accession NM_032568) is another VGAM1005 host target gene. GABARAPL3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by GABARAPL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABARAPL3 BINDING SITE, designated SEQ ID:26298, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37161] Another function of VGAM1005 is therefore inhibition of GABA(A) Receptors Associated Protein Like 3 (GABARAPL3, Accession NM_032568). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABARAPL3. KIAA0668 (Accession XM_039332) is another VGAM1005 host target gene. KIAA0668 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0668 BINDING SITE, designated SEQ ID:33048, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37162] Another function of VGAM1005 is therefore inhibition of

KIAA0668 (Accession XM_039332). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0668. KIAA0997 (Accession NM_014950) is another VGAM1005 host target gene. KIAA0997 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0997 BINDING SITE, designated SEQ ID:17281, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37163] Another function of VGAM1005 is therefore inhibition of KIAA0997 (Accession NM_014950). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0997. KIAA1228 (Accession XM_036408) is another VGAM1005 host target gene. KIAA1228 BINDING SITE1 and KIAA1228 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1228, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1228 BINDING SITE1 and KIAA1228 BINDING SITE2, designated SEQ ID:32440 and SEQ ID:32441 respectively, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37164] Another function of VGAM1005 is therefore inhibition of KIAA1228 (Accession XM_036408). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1228. PC4 and SFRS1 Interacting Protein 2 (PSIP2, Accession NM_033222) is another VGAM1005 host target gene. PSIP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PSIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSIP2 BINDING SITE, designated SEQ ID:27067, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37165] Another function of VGAM1005 is therefore inhibition of PC4 and SFRS1 Interacting Protein 2 (PSIP2, Accession NM_033222). Accordingly, utilities of VGAM1005 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PSIP2. Prostaglandin E Synthase 2 (PTGES2, Accession NM_025072) is another VGAM1005 host target gene. PTGES2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTGES2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGES2 BINDING SITE, designated SEQ ID:24669, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37166] Another function of VGAM1005 is therefore inhibition of Prostaglandin E Synthase 2 (PTGES2, Accession NM_025072). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGES2. Rab11-FIP3 (Accession NM_014700) is another VGAM1005 host target gene. Rab11-FIP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by Rab11-FIP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of Rab11–FIP3 BINDING SITE, designated SEQ ID:16227, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37167] Another function of VGAM1005 is therefore inhibition of Rab11–FIP3 (Accession NM_014700). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11–FIP3. RAP2B, Member of RAS Oncogene Family (RAP2B, Accession XM_171061) is another VGAM1005 host target gene. RAP2B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAP2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP2B BINDING SITE, designated SEQ ID:45861, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37168] Another function of VGAM1005 is therefore inhibition of RAP2B, Member of RAS Oncogene Family (RAP2B, Accession XM_171061). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with RAP2B. Rho-related BTB Domain Containing 1 (RHOBTB1, Accession XM_166144) is another VGAM1005 host target gene. RHOBTB1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RHOBTB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB1 BINDING SITE, designated SEQ ID:43951, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37169] Another function of VGAM1005 is therefore inhibition of Rho-related BTB Domain Containing 1 (RHOBTB1, Accession XM_166144). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB1. RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM_017495) is another VGAM1005 host target gene. RNPC1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RNPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of RNPC1 BINDING SITE, designated SEQ ID:18957, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37170] Another function of VGAM1005 is therefore inhibition of RNA-binding Region (RNP1, RRM) Containing 1 (RNPC1, Accession NM_017495). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPC1. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379) is another VGAM1005 host target gene. SEMA3C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3C BINDING SITE, designated SEQ ID:13073, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37171] Another function of VGAM1005 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Short Basic

Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3C. Williams–Beuren Syndrome Chromosome Region 23 (WBSCR23, Accession NM_025042) is another VGAM1005 host target gene. WBSCR23 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by WBSCR23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR23 BINDING SITE, designated SEQ ID:24638, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37172] Another function of VGAM1005 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 23 (WBSCR23, Accession NM_025042). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR23. LOC133308 (Accession XM_059638) is another VGAM1005 host target gene. LOC133308 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by LOC133308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133308 BINDING SITE, designated SEQ ID:37035, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37173] Another function of VGAM1005 is therefore inhibition of LOC133308 (Accession XM_059638). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133308. LOC134145 (Accession XM_059691) is another VGAM1005 host target gene. LOC134145 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC134145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134145 BINDING SITE, designated SEQ ID:37062, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37174] Another function of VGAM1005 is therefore inhibition of LOC134145 (Accession XM_059691). Accordingly, utilities

of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134145. LOC143915 (Accession XM_096502) is another VGAM1005 host target gene. LOC143915 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143915 BINDING SITE, designated SEQ ID:40377, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37175] Another function of VGAM1005 is therefore inhibition of LOC143915 (Accession XM_096502). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143915. LOC145481 (Accession XM_085163) is another VGAM1005 host target gene. LOC145481 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145481 BINDING SITE, designated SEQ ID:37890, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37176] Another function of VGAM1005 is therefore inhibition of LOC145481 (Accession XM_085163). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145481. LOC146894 (Accession NM_145273) is another VGAM1005 host target gene. LOC146894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146894 BINDING SITE, designated SEQ ID:29781, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37177] Another function of VGAM1005 is therefore inhibition of LOC146894 (Accession NM_145273). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146894. LOC148709 (Accession XM_086281) is another VGAM1005 host target gene. LOC148709 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148709 BINDING SITE, designated SEQ ID:38583, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37178] Another function of VGAM1005 is therefore inhibition of LOC148709 (Accession XM_086281). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148709. LOC149297 (Accession XM_097622) is another VGAM1005 host target gene. LOC149297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149297 BINDING SITE, designated SEQ ID:40979, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37179] Another function of VGAM1005 is therefore inhibition of

LOC149297 (Accession XM_097622). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149297. LOC151127 (Accession XM_087104) is another VGAM1005 host target gene. LOC151127 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151127 BINDING SITE, designated SEQ ID:39061, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37180] Another function of VGAM1005 is therefore inhibition of LOC151127 (Accession XM_087104). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151127. LOC153474 (Accession XM_087684) is another VGAM1005 host target gene. LOC153474 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC153474 BINDING SITE, designated SEQ ID:39379, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37181] Another function of VGAM1005 is therefore inhibition of LOC153474 (Accession XM_087684). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153474. LOC153505 (Accession XM_087693) is another VGAM1005 host target gene. LOC153505 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153505 BINDING SITE, designated SEQ ID:39382, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37182] Another function of VGAM1005 is therefore inhibition of LOC153505 (Accession XM_087693). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153505. LOC164537 (Accession XM_104534) is an-

other VGAM1005 host target gene. LOC164537 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164537 BINDING SITE, designated SEQ ID:42172, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37183] Another function of VGAM1005 is therefore inhibition of LOC164537 (Accession XM_104534). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164537. LOC219513 (Accession XM_169166) is another VGAM1005 host target gene. LOC219513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219513 BINDING SITE, designated SEQ ID:45294, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37184] Another function of VGAM1005 is therefore inhibition of LOC219513 (Accession XM_169166). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219513. LOC221938 (Accession XM_166542) is another VGAM1005 host target gene. LOC221938 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221938 BINDING SITE, designated SEQ ID:44513, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37185] Another function of VGAM1005 is therefore inhibition of LOC221938 (Accession XM_166542). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221938. LOC255104 (Accession XM_170911) is another VGAM1005 host target gene. LOC255104 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255104, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255104 BINDING SITE, designated SEQ ID:45684, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37186] Another function of VGAM1005 is therefore inhibition of LOC255104 (Accession XM_170911). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255104. LOC257541 (Accession XM_175175) is another VGAM1005 host target gene. LOC257541 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257541, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257541 BINDING SITE, designated SEQ ID:46671, to the nucleotide sequence of VGAM1005 RNA, herein designated VGAM RNA, also designated SEQ ID:3716.

[37187] Another function of VGAM1005 is therefore inhibition of LOC257541 (Accession XM_175175). Accordingly, utilities of VGAM1005 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC257541. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1006 (VGAM1006) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37188] VGAM1006 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1006 was detected is described hereinabove with reference to Figs. 1–8.

[37189] VGAM1006 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37190] VGAM1006 gene encodes a VGAM1006 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1006 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1006 precursor RNA is designated SEQ ID:992, and is provided hereinbelow with refer–

ence to the sequence listing part. Nucleotide sequence SEQ ID:992 is located at position 197086 relative to the genome of Chimpanzee Cytomegalovirus.

- [37191] VGAM1006 precursor RNA folds onto itself, forming VGAM1006 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [37192] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1006 folded precursor RNA into VGAM1006 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1006 RNA is designated SEQ ID:3717, and is provided hereinbelow with reference to the sequence listing part.

[37193] VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1006 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37194] VGAM1006 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1006 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1006 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37195] The complementary binding of VGAM1006 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1006 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1006 host target RNA into VGAM1006 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37196] It is appreciated that VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1006 host target genes. The mRNA of each one of this plurality of VGAM1006 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1006 RNA, herein designated VGAM RNA, and which when bound by VGAM1006 RNA causes

inhibition of translation of respective one or more VGAM1006 host target proteins.

[37197] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1006 gene, herein designated VGAM GENE, on one or more VGAM1006 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37198] It is yet further appreciated that a function of VGAM1006 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1006 include diagnosis, prevention and

treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1006 correlate with, and may be deduced from, the identity of the host target genes which VGAM1006 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37199] Nucleotide sequences of the VGAM1006 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1006 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1006 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1006 are further described hereinbelow with reference to Table 1.

[37200] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1006 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1006 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37201] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1006 gene, herein designated VGAM is inhibition of expression of VGAM1006 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1006 correlate with, and may be deduced from, the identity of the target genes which VGAM1006 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37202] Acyl-Coenzyme A Dehydrogenase, C-4 to C-12 Straight Chain (ACADM, Accession NM_000016) is a VGAM1006 host target gene. ACADM BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ACADM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADM BINDING SITE, designated SEQ ID:5451, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37203] A function of VGAM1006 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, C-4 to C-12 Straight Chain (ACADM, Accession NM_000016). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADM. AF5Q31 (Accession NM_014423) is another VGAM1006 host target gene. AF5Q31 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AF5Q31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF5Q31 BINDING SITE, designated SEQ ID:15777, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37204] Another function of VGAM1006 is therefore inhibition of AF5Q31 (Accession NM_014423). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF5Q31. Asialoglycoprotein Receptor 2 (ASGR2, Accession NM_080912) is another VGAM1006 host target gene. ASGR2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ASGR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASGR2 BINDING SITE, designated SEQ ID:28130, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37205] Another function of VGAM1006 is therefore inhibition of Asialoglycoprotein Receptor 2 (ASGR2, Accession NM_080912). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASGR2. BarH-like 1 (Drosophila) (BARHL1, Accession NM_020064) is another VGAM1006 host target gene. BARHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BARHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BARHL1 BINDING SITE, designated SEQ ID:21300, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37206] Another function of VGAM1006 is therefore inhibition of BarH-like 1 (Drosophila) (BARHL1, Accession NM_020064), a gene which controls the expression of neural adhesion molecules. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BARHL1. The function of BARHL1 has been established by previous studies. The BarH1 and BarH2 (Bar) Drosophila genes are homeobox-

containing genes, which are required for the fate determination of external sensory organs in the fly. Using a bioinformatic approach, Bulfone et al. (2000) identified murine and human homeobox genes highly related to the Bar *Drosophila* genes, which they designated Barhl1 and Barhl2 (OMIM Ref. No. 605212). Bulfone et al. (2000) screened a human lambda genomic library and identified a clone containing the last 2 exons of the BARHL1 gene. By joining these 2 exons together, they obtained a partial BARHL1 sequence (GenBank AJ237816) containing the homeobox and stop codon. This partial BARHL1 sequence and the corresponding mouse sequence share 99% amino acid identity. The mouse Barhl1 gene is more highly homologous to *Drosophila* BARH1 than is the murine Barx1 gene (OMIM Ref. No. 603260). In situ hybridization to mouse tissues at several developmental stages revealed that Barhl1 is exclusively expressed in restricted domains of the developing central nervous system, in particular the diencephalon and rhombencephalon, where it is expressed in migrating cells giving rise to the cerebellar external granular layer and to specific populations of dorsal sensory interneurons of the spinal cord. The authors hypothesized that Barhl1 function may be required for the

generation of these specific subtypes of neuronal progenitors. Bulfone et al. (2000) stated that the mapping assignment and the expression pattern make BARHL1 a positional candidate gene for a form of Joubert syndrome (OMIM Ref. No. 213300), a rare developmental anomaly of the cerebellum in humans. Blair et al. (2002) appeared to have excluded BARHL1 as the site of the mutation in the form of Joubert syndrome that is linked to 9q34.

[37207] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37208] Bulfone, A.; Menguzzato, E.; Broccoli, V.; Marchitello, A.; Gattuso, C.; Mariani, M.; Consalez, G. G.; Martinez, S.; Bal-labio, A.; Banfi, S. : Barhl1, a gene belonging to a new subfamily of mammalian homeobox genes, is expressed in migrating neurons of the CNS. Hum. Molec. Genet. 9: 1443–1452, 2000. ; and

[37209] Blair, I. P.; Gibson, R. R.; Bennett, C. L.; Chance, P. F. : Search for genes involved in Joubert syndrome: evidence that one or more major loci are yet to be identified and exclusion o.

[37210] Further studies establishing the function and utilities of BARHL1 are found in John Hopkins OMIM database record

ID 605211, and in cited publications numbered 9538 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CGTHBA (Accession NM_012075) is another VGAM1006 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14362, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37211] Another function of VGAM1006 is therefore inhibition of CGTHBA (Accession NM_012075). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372) is another VGAM1006 host target gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15021, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37212] Another function of VGAM1006 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28.Espin (ESPN, Accession NM_031475) is another VGAM1006 host target gene. ESPN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESPN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESPN BINDING SITE, designated SEQ ID:25549, to the nucleotide sequence of VGAM1006 RNA, herein designated

VGAM RNA, also designated SEQ ID:3717.

[37213] Another function of VGAM1006 is therefore inhibition of Espin (ESPN, Accession NM_031475), a gene which a membrane-cytoskeletal assemblages . Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESPN. The function of ESPN has been established by previous studies. Ectoplasmic specializations are membrane-cytoskeletal assemblages found in Sertoli cells at sites of attachment to elongate spermatids or neighboring Sertoli cells. Bartles et al. (1996) identified the rat actin-bundling protein espin, which is localized to ectoplasmic specializations. The 836-amino acid espin protein had a molecular mass of approximately 110 kD in SDS gels. Northern blot analysis detected a 2.9-kb espin transcript only in rat testis; a minor 1.7-kb transcript was detected in small intestine and kidney. Bartles et al. (1998) identified a 30-kD, 253-amino acid isoform of rat espin that localized to brush border microvilli in the intestine and kidney. Espin and small espin share a 167-amino acid C-terminal peptide that includes a 116-amino acid C-terminal actin-bundling module that is necessary and sufficient for actin bundle formation in vitro; however, they

contain different N termini. Bartles et al. (1998) and Chen et al. (1999) determined that unlike many actin-bundling proteins, the rat espins bind actin filaments with high affinity, and their actin-bundling activities are not inhibited by calcium. Zheng et al. (2000) determined that espins are present in hair cell stereocilia and uncovered a connection between the espin gene and jerker mouse, a recessive mutation that causes hair cell degeneration, deafness, and vestibular dysfunction. The tissues of jerker mice did not accumulate espin proteins but contained normal levels of espin mRNAs. The authors identified a frameshift mutation in the espin gene of jerker mice that affected the espin C-terminal actin-bundling module. These data suggested that jerker mice are espin null and that the jerker phenotype results from a mutation in the espin gene. Animal model experiments lend further support to the function of ESPN. Zheng et al. (2000) determined that espins are present in hair cell stereocilia and uncovered a connection between the espin gene and jerker mouse, a recessive mutation that causes hair cell degeneration, deafness, and vestibular dysfunction. The tissues of jerker mice did not accumulate espin proteins but contained normal levels of espin mRNAs. The authors

identified a frameshift mutation in the espin gene of jerker mice that affected the espin C-terminal actin-bundling module. These data suggested that jerker mice are espin null and that the jerker phenotype results from a mutation in the espin gene.

[37214] It is appreciated that the abovementioned animal model for ESPN is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[37215] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37216] Chen, B.; Li, A.; Wang, D.; Wang, M.; Zheng, L.; Bartles, J. R. : Espin contains an additional actin-binding site in its N terminus and is a major actin-bundling protein of the Sertoli cell-spermatid ectoplasmic specialization junctional plaque. *Molec. Biol. Cell* 10: 4327-4339, 1999. ; and

[37217] Zheng, L.; Sekerkova, G.; Vranich, K.; Tilney, L. G.; Mugnaini, E.; Bartles, J. R. : The deaf jerker mouse has a mutation in the gene encoding the espin actin-bundling proteins of hair.

[37218] Further studies establishing the function and utilities of ESPN are found in John Hopkins OMIM database record ID

606351, and in cited publications numbered 6421–6424 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glypican 1 (GPC1, Accession NM_002081) is another VGAM1006 host target gene. GPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC1 BINDING SITE, designated SEQ ID:7872, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37219] Another function of VGAM1006 is therefore inhibition of Glypican 1 (GPC1, Accession NM_002081), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC1. The function of GPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. HTRA3 (Accession XM_114416) is another VGAM1006 host target gene. HTRA3 BINDING SITE is HOST TARGET binding site found

in the 5' untranslated region of mRNA encoded by HTRA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTRA3 BINDING SITE, designated SEQ ID:42941, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37220] Another function of VGAM1006 is therefore inhibition of HTRA3 (Accession XM_114416). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTRA3. Insulin-like Growth Factor 2 (somatomedin A) (IGF2, Accession NM_000612) is another VGAM1006 host target gene. IGF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2 BINDING SITE, designated SEQ ID:6215, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37221] Another function of VGAM1006 is therefore inhibition of

Insulin-like Growth Factor 2 (somatomedin A) (IGF2, Accession NM_000612). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2. Kinesin Family Member C3 (KIFC3, Accession NM_005550) is another VGAM1006 host target gene. KIFC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIFC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIFC3 BINDING SITE, designated SEQ ID:12082, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37222] Another function of VGAM1006 is therefore inhibition of Kinesin Family Member C3 (KIFC3, Accession NM_005550), a gene which may function in intracellular transport and mitosis. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIFC3. The function of KIFC3 has been established by previous studies. Kinesins comprise a large superfamily of molecular motors that use the energy of ATP hydrolysis to translocate

cargoes along microtubules. Members share extensive homology within a globular domain containing the microtubule- and ATP-binding sites and have a coiled-coil stalk domain that mediates oligomerization. Different kinesin family members participate in specific and diverse motile processes, such as cell division, organelle transport, and nuclear movement. Motile processes are essential to the function, morphogenesis, and maintenance of photoreceptors and the retinal pigment epithelium (RPE). By PCR of human retina cDNA using degenerate oligonucleotides based on highly conserved sequences in the kinesin motor domain, Hoang et al. (1998) isolated cDNAs encoding 4 different kinesin family members, including KIFC3. KIFC3 is highly homologous to mouse *Kifc3* and Morone saxatilis (striped bass) FKIF2, which was the most abundant kinesin identified in both the retina and RPE (Bost-Usinger et al., 1997). The predicted 687-amino acid KIFC3 protein contains the highly conserved ATP/GTP-binding site, or P-loop, and kinesin motor domain. In contrast to conventional kinesin and kinesin families that have N-terminal motor domains, the motor domains of human KIFC3, mouse *Kifc3*, and FKIF2 are predicted to reside at the C-terminal end; such kinesins are termed C-kinesins. An an-

tibody raised against FKIF2 recognized an approximately 80-kD protein in human retina, RPE, kidney, and lung

[37223] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37224] Bost-Usinger, L.; Chen, R. J.; Hillman, D.; Park, P.; Burnside, B. : Multiple kinesin family members expressed in teleost retina and RPE include a novel C-terminal kinesin. *Exp. Eye Res.* 64: 781–794, 1997. ; and

[37225] Hoang, E. H.; Whitehead, J. L.; Dose, A. C.; Burnside, B. : Cloning of a novel C-terminal kinesin (KIFC3) that maps to human chromosome 16q13–q21 and thus is a candidate gene for Bardet.

[37226] Further studies establishing the function and utilities of KIFC3 are found in John Hopkins OMIM database record ID 604535, and in cited publications numbered 7462–7463 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Notch Homolog 3 (Drosophila) (NOTCH3, Accession NM_000435) is another VGAM1006 host target gene. NOTCH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NOTCH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND–

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOTCH3 BINDING SITE, designated SEQ ID:6016, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37227] Another function of VGAM1006 is therefore inhibition of Notch Homolog 3 (Drosophila) (NOTCH3, Accession NM_000435), a gene which may function in cell fate specification during development. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOTCH3. The function of NOTCH3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128.PACE (Accession NM_002569) is another VGAM1006 host target gene. PACE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE BINDING SITE, designated SEQ ID:8426, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA,

also designated SEQ ID:3717.

[37228] Another function of VGAM1006 is therefore inhibition of PACE (Accession NM_002569), a gene which processes pro-parathyroid hormone, pro-transforming growth factor beta. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE. The function of PACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM151. Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM_166424) is another VGAM1006 host target gene. PACSIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN1 BINDING SITE, designated SEQ ID:44310, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37229] Another function of VGAM1006 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 1

(PACSIN1, Accession XM_166424). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN1. Retinoic Acid Receptor, Alpha (RARA, Accession NM_000964) is another VGAM1006 host target gene. RARA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RARA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RARA BINDING SITE, designated SEQ ID:6688, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37230] Another function of VGAM1006 is therefore inhibition of Retinoic Acid Receptor, Alpha (RARA, Accession NM_000964). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RARA. RNA (guanine-7-) Methyltransferase (RNMT, Accession NM_003799) is another VGAM1006 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9885, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37231] Another function of VGAM1006 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM_004560) is another VGAM1006 host target gene. ROR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ROR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROR2 BINDING SITE, designated SEQ ID:10898, to the nucleotide sequence of

VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37232] Another function of VGAM1006 is therefore inhibition of Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM_004560), a gene which may be involved in the early formayion of the chonrocytes. Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROR2. The function of ROR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232.Cat Eye Syndrome Chromosome Region, Candidate 2 (CECR2, Accession NM_031413) is another VGAM1006 host target gene. CECR2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CECR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR2 BINDING SITE, designated SEQ ID:25393, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37233] Another function of VGAM1006 is therefore inhibition of

Cat Eye Syndrome Chromosome Region, Candidate 2 (CECR2, Accession NM_031413). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR2. CEP3 (Accession NM_006449) is another VGAM1006 host target gene. CEP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CEP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP3 BINDING SITE, designated SEQ ID:13158, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37234] Another function of VGAM1006 is therefore inhibition of CEP3 (Accession NM_006449). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP3. DKFZP434H132 (Accession XM_057020) is another VGAM1006 host target gene. DKFZP434H132 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434H132, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H132 BINDING SITE, designated SEQ ID:36449, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37235] Another function of VGAM1006 is therefore inhibition of DKFZP434H132 (Accession XM_057020). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H132. DKFZp547M072 (Accession XM_028067) is another VGAM1006 host target gene. DKFZp547M072 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547M072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547M072 BINDING SITE, designated SEQ ID:30616, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37236] Another function of VGAM1006 is therefore inhibition of DKFZp547M072 (Accession XM_028067). Accordingly,

utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547M072. DKFZp586I021 (Accession NM_032271) is another VGAM1006 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26026, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37237] Another function of VGAM1006 is therefore inhibition of DKFZp586I021 (Accession NM_032271). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. FLJ10743 (Accession NM_018201) is another VGAM1006 host target gene. FLJ10743 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ10743 BINDING SITE, designated SEQ ID:20079, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37238] Another function of VGAM1006 is therefore inhibition of FLJ10743 (Accession NM_018201). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10743. FLJ14810 (Accession NM_032843) is another VGAM1006 host target gene. FLJ14810 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14810 BINDING SITE, designated SEQ ID:26635, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37239] Another function of VGAM1006 is therefore inhibition of FLJ14810 (Accession NM_032843). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14810. FLJ21438 (Accession XM_029084) is another

VGAM1006 host target gene. FLJ21438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21438 BINDING SITE, designated SEQ ID:30848, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37240] Another function of VGAM1006 is therefore inhibition of FLJ21438 (Accession XM_029084). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21438. FLJ22215 (Accession NM_022834) is another VGAM1006 host target gene. FLJ22215 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22215 BINDING SITE, designated SEQ ID:23117, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37241] Another function of VGAM1006 is therefore inhibition of FLJ22215 (Accession NM_022834). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22215. KIAA0258 (Accession NM_014785) is another VGAM1006 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16647, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37242] Another function of VGAM1006 is therefore inhibition of KIAA0258 (Accession NM_014785). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA0552 (Accession NM_014731) is another VGAM1006 host target gene. KIAA0552 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0552, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0552 BINDING SITE, designated SEQ ID:16348, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37243] Another function of VGAM1006 is therefore inhibition of KIAA0552 (Accession NM_014731). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0552. KIAA0618 (Accession NM_014833) is another VGAM1006 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16834, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37244] Another function of VGAM1006 is therefore inhibition of KIAA0618 (Accession NM_014833). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0618. KIAA1530 (Accession XM_042661) is another VGAM1006 host target gene. KIAA1530 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1530, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1530 BINDING SITE, designated SEQ ID:33734, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37245] Another function of VGAM1006 is therefore inhibition of KIAA1530 (Accession XM_042661). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1530. MCLC (Accession NM_015127) is another VGAM1006 host target gene. MCLC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCLC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCLC BINDING SITE, designated SEQ ID:17492, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3717.

[37246] Another function of VGAM1006 is therefore inhibition of MCLC (Accession NM_015127). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCLC. QKI (Accession XM_037438) is another VGAM1006 host target gene. QKI BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by QKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of QKI BINDING SITE, designated SEQ ID:32617, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37247] Another function of VGAM1006 is therefore inhibition of QKI (Accession XM_037438). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with QKI. RBAK (Accession NM_021163) is another VGAM1006 host target gene. RBAK BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RBAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RBAK BINDING SITE, designated SEQ ID:22141, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37248] Another function of VGAM1006 is therefore inhibition of RBAK (Accession NM_021163). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBAK. LOC116113 (Accession XM_166413) is another VGAM1006 host target gene. LOC116113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116113 BINDING SITE, designated SEQ ID:44287, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37249] Another function of VGAM1006 is therefore inhibition of LOC116113 (Accession XM_166413). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC116113. LOC145547 (Accession XM_085167) is another VGAM1006 host target gene. LOC145547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145547 BINDING SITE, designated SEQ ID:37893, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37250] Another function of VGAM1006 is therefore inhibition of LOC145547 (Accession XM_085167). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145547. LOC221424 (Accession XM_168060) is another VGAM1006 host target gene. LOC221424 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221424, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221424 BINDING SITE, designated SEQ ID:44979, to the nucleotide sequence of VGAM1006 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3717.

[37251] Another function of VGAM1006 is therefore inhibition of LOC221424 (Accession XM_168060). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221424. LOC221486 (Accession XM_165760) is another VGAM1006 host target gene. LOC221486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221486 BINDING SITE, designated SEQ ID:43743, to the nucleotide sequence of VGAM1006 RNA, herein designated VGAM RNA, also designated SEQ ID:3717.

[37252] Another function of VGAM1006 is therefore inhibition of LOC221486 (Accession XM_165760). Accordingly, utilities of VGAM1006 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221486. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1007 (VGAM1007) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37253] VGAM1007 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1007 was detected is described hereinabove with reference to Figs. 1–8.

[37254] VGAM1007 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37255] VGAM1007 gene encodes a VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1007 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1007 precursor RNA is designated SEQ ID:993, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:993 is located at position 200001 relative to the genome of Chimpanzee Cytomegalovirus.

[37256] VGAM1007 precursor RNA folds onto itself, forming

VGAM1007 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37257] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1007 folded precursor RNA into VGAM1007 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1007 RNA is designated SEQ ID:3718, and is provided hereinbelow with reference to the sequence listing part.

[37258] VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1007 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37259] VGAM1007 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1007 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1007 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37260] The complementary binding of VGAM1007 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1007 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1007 host target RNA into VGAM1007 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37261] It is appreciated that VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1007 host target genes. The mRNA of each one of this plurality of VGAM1007 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1007 RNA, herein designated VGAM RNA, and which when bound by VGAM1007 RNA causes inhibition of translation of respective one or more VGAM1007 host target proteins.

[37262] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1007 gene, herein designated VGAM GENE, on one or more VGAM1007 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37263] It is yet further appreciated that a function of VGAM1007 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1007 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1007 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37264] Nucleotide sequences of the VGAM1007 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1007 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1007 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1007 are further described hereinbelow with reference to Table 1.

[37265] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1007 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1007 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37266] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1007 gene, herein designated VGAM is inhibition of expression of VGAM1007 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1007 correlate with, and may be deduced from, the identity of the target genes which VGAM1007 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[37267] E1A Binding Protein P300 (EP300, Accession NM_001429) is a VGAM1007 host target gene. EP300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EP300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EP300 BINDING SITE, designated SEQ ID:7150, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37268] A function of VGAM1007 is therefore inhibition of E1A Binding Protein P300 (EP300, Accession NM_001429), a gene which may have a function in cell cycle regulation. Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EP300. The function of EP300 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. GRB2-associated Binding Protein 2 (GAB2, Accession NM_012296) is another VGAM1007 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:14653 and SEQ ID:27848 respectively, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37269] Another function of VGAM1007 is therefore inhibition of GRB2-associated Binding Protein 2 (GAB2, Accession NM_012296), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53. Transducin (beta)-like 2 (TBL2, Accession NM_032988) is another VGAM1007 host target gene. TBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TBL2 BINDING SITE, designated SEQ ID:26869, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37270] Another function of VGAM1007 is therefore inhibition of Transducin (beta)-like 2 (TBL2, Accession NM_032988), a gene which is of unknown function. Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL2. The function of TBL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM1007 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25516, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37271] Another function of VGAM1007 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332) is another VGAM1007 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:27168, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37272] Another function of VGAM1007 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. DGS-A (Accession XM_097827) is another VGAM1007 host target gene. DGS-A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by DGS-A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGS-A BINDING SITE, designated SEQ ID:41149, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37273] Another function of VGAM1007 is therefore inhibition of DGS-A (Accession XM_097827). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGS-A. DKFZP761E2110 (Accession NM_030953) is another VGAM1007 host target gene. DKFZP761E2110 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP761E2110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761E2110 BINDING SITE, designated SEQ ID:25226, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37274] Another function of VGAM1007 is therefore inhibition of

DKFZP761E2110 (Accession NM_030953). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761E2110. HCCA2 (Accession XM_039894) is another VGAM1007 host target gene. HCCA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HCCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCCA2 BINDING SITE, designated SEQ ID:33205, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37275] Another function of VGAM1007 is therefore inhibition of HCCA2 (Accession XM_039894). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCCA2. KIAA0449 (Accession NM_017596) is another VGAM1007 host target gene. KIAA0449 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0449 BINDING SITE, designated SEQ ID:19053, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37276] Another function of VGAM1007 is therefore inhibition of KIAA0449 (Accession NM_017596). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0449. KIAA0596 (Accession XM_031706) is another VGAM1007 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE, designated SEQ ID:31462, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37277] Another function of VGAM1007 is therefore inhibition of KIAA0596 (Accession XM_031706). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. KIAA0599 (Accession XM_085127) is another

VGAM1007 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37858, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37278] Another function of VGAM1007 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA1283 (Accession XM_050563) is another VGAM1007 host target gene. KIAA1283 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1283 BINDING SITE, designated SEQ ID:35663, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37279] Another function of VGAM1007 is therefore inhibition of KIAA1283 (Accession XM_050563). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1283. MGC2217 (Accession NM_024300) is another VGAM1007 host target gene. MGC2217 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2217 BINDING SITE, designated SEQ ID:23589, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37280] Another function of VGAM1007 is therefore inhibition of MGC2217 (Accession NM_024300). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2217. LOC114932 (Accession XM_052614) is another VGAM1007 host target gene. LOC114932 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC114932, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114932 BINDING SITE, designated SEQ ID:36006, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37281] Another function of VGAM1007 is therefore inhibition of LOC114932 (Accession XM_052614). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114932. LOC159036 (Accession XM_099018) is another VGAM1007 host target gene. LOC159036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159036 BINDING SITE, designated SEQ ID:42053, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37282] Another function of VGAM1007 is therefore inhibition of LOC159036 (Accession XM_099018). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC159036. LOC201595 (Accession XM_114346) is another VGAM1007 host target gene. LOC201595 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201595, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201595 BINDING SITE, designated SEQ ID:42886, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37283] Another function of VGAM1007 is therefore inhibition of LOC201595 (Accession XM_114346). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201595. LOC222662 (Accession XM_167086) is another VGAM1007 host target gene. LOC222662 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222662 BINDING SITE, designated SEQ ID:44603, to the nucleotide sequence of VGAM1007 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3718.

[37284] Another function of VGAM1007 is therefore inhibition of LOC222662 (Accession XM_167086). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222662. LOC256586 (Accession XM_170759) is another VGAM1007 host target gene. LOC256586 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256586, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256586 BINDING SITE, designated SEQ ID:45515, to the nucleotide sequence of VGAM1007 RNA, herein designated VGAM RNA, also designated SEQ ID:3718.

[37285] Another function of VGAM1007 is therefore inhibition of LOC256586 (Accession XM_170759). Accordingly, utilities of VGAM1007 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256586. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1008 (VGAM1008) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37286] VGAM1008 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1008 was detected is described hereinabove with reference to Figs. 1-8.

[37287] VGAM1008 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37288] VGAM1008 gene encodes a VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1008 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1008 precursor RNA is designated SEQ ID:994, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:994 is located at position 199188 relative to the genome of Chimpanzee Cytomegalovirus.

[37289] VGAM1008 precursor RNA folds onto itself, forming

VGAM1008 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37290] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1008 folded precursor RNA into VGAM1008 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1008 RNA is designated SEQ ID:3719, and is provided hereinbelow with reference to the sequence listing part.

[37291] VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1008 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37292] VGAM1008 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1008 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1008 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37293] The complementary binding of VGAM1008 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1008 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1008 host target RNA into VGAM1008 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37294] It is appreciated that VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1008 host target genes. The mRNA of each one of this plurality of VGAM1008 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1008 RNA, herein designated VGAM RNA, and which when bound by VGAM1008 RNA causes inhibition of translation of respective one or more VGAM1008 host target proteins.

[37295] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1008 gene, herein designated VGAM GENE, on one or more VGAM1008 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37296] It is yet further appreciated that a function of VGAM1008 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1008 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1008 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37297] Nucleotide sequences of the VGAM1008 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1008 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1008 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1008 are further described hereinbelow with reference to Table 1.

[37298] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1008 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1008 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37299] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1008 gene, herein designated VGAM is inhibition of expression of VGAM1008 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1008 correlate with, and may be deduced from, the identity of the target genes which VGAM1008 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[37300] Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507) is a VGAM1008 host target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, designated SEQ ID:8336, to the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, also designated SEQ ID:3719.

[37301] A function of VGAM1008 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM212. Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Ac-

cession NM_025136) is another VGAM1008 host target gene. OPA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA3 BINDING SITE, designated SEQ ID:24775, to the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, also designated SEQ ID:3719.

[37302] Another function of VGAM1008 is therefore inhibition of Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Accession NM_025136). Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA3. KIAA0447 (Accession XM_049733) is another VGAM1008 host target gene. KIAA0447 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35492, to the nucleotide sequence of VGAM1008 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3719.

[37303] Another function of VGAM1008 is therefore inhibition of KIAA0447 (Accession XM_049733). Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635) is another VGAM1008 host target gene. P2RX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RX1 BINDING SITE, designated SEQ ID:33353, to the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, also designated SEQ ID:3719.

[37304] Another function of VGAM1008 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635). Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RX1. Ubiquitin Specific Protease 22 (USP22, Accession XM_042698) is another VGAM1008 host target gene.

USP22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP22 BINDING SITE, designated SEQ ID:33752, to the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, also designated SEQ ID:3719.

[37305] Another function of VGAM1008 is therefore inhibition of Ubiquitin Specific Protease 22 (USP22, Accession XM_042698). Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP22. LOC146229 (Accession XM_085387) is another VGAM1008 host target gene. LOC146229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146229 BINDING SITE, designated SEQ ID:38118, to the nucleotide sequence of VGAM1008 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3719.

[37306] Another function of VGAM1008 is therefore inhibition of LOC146229 (Accession XM_085387). Accordingly, utilities of VGAM1008 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146229. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1009 (VGAM1009) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37307] VGAM1009 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1009 was detected is described hereinabove with reference to Figs. 1–8.

[37308] VGAM1009 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37309] VGAM1009 gene encodes a VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1009 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1009 precursor RNA is designated SEQ ID:995, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:995 is located at position 31121 relative to the genome of Equine Herpesvirus 4.

- [37310] VGAM1009 precursor RNA folds onto itself, forming VGAM1009 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [37311] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1009 folded precursor RNA into VGAM1009 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1009 RNA is designated SEQ ID:3720, and is provided hereinbelow with reference to the sequence listing part.

[37312] VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1009 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37313] VGAM1009 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1009 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1009 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37314] The complementary binding of VGAM1009 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1009 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1009 host target RNA into VGAM1009 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37315] It is appreciated that VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1009 host target genes. The mRNA of

each one of this plurality of VGAM1009 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1009 RNA, herein designated VGAM RNA, and which when bound by VGAM1009 RNA causes inhibition of translation of respective one or more VGAM1009 host target proteins.

[37316] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1009 gene, herein designated VGAM GENE, on one or more VGAM1009 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[37317] It is yet further appreciated that a function of VGAM1009 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1009 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1009 correlate with, and may be deduced from, the identity of the host target genes which VGAM1009 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37318] Nucleotide sequences of the VGAM1009 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1009 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1009 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1009 are further described hereinbelow with reference to Table 1.

[37319] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1009 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1009 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37320] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1009 gene, herein designated VGAM is inhibition of expression of VGAM1009 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1009 correlate with, and may be deduced from, the identity of the target genes which VGAM1009 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37321] Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275) is a VGAM1009 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14599, to the nucleotide sequence of VGAM1009 RNA, herein designated VGAM RNA, also designated SEQ ID:3720.

[37322] A function of VGAM1009 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275), a gene which is a novel interleukin-1 recep-

tor antagonist gene. Accordingly, utilities of VGAM1009 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263.NBR2 (Accession NM_005821) is another VGAM1009 host target gene. NBR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBR2 BINDING SITE, designated SEQ ID:12424, to the nucleotide sequence of VGAM1009 RNA, herein designated VGAM RNA, also designated SEQ ID:3720.

[37323] Another function of VGAM1009 is therefore inhibition of NBR2 (Accession NM_005821). Accordingly, utilities of VGAM1009 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBR2. LOC149134 (Accession XM_097594) is another VGAM1009 host target gene. LOC149134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC149134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149134 BINDING SITE, designated SEQ ID:40957, to the nucleotide sequence of VGAM1009 RNA, herein designated VGAM RNA, also designated SEQ ID:3720.

[37324] Another function of VGAM1009 is therefore inhibition of LOC149134 (Accession XM_097594). Accordingly, utilities of VGAM1009 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149134. LOC168283 (Accession XM_094966) is another VGAM1009 host target gene. LOC168283 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168283 BINDING SITE, designated SEQ ID:40239, to the nucleotide sequence of VGAM1009 RNA, herein designated VGAM RNA, also designated SEQ ID:3720.

[37325] Another function of VGAM1009 is therefore inhibition of LOC168283 (Accession XM_094966). Accordingly, utilities

of VGAM1009 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168283. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1010 (VGAM1010) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37326] VGAM1010 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1010 was detected is described hereinabove with reference to Figs. 1–8.

[37327] VGAM1010 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37328] VGAM1010 gene encodes a VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1010 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1010 precursor RNA is designated SEQ ID:996, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:996 is located at position 29765 relative to the genome of Equine Herpesvirus 4.

[37329] VGAM1010 precursor RNA folds onto itself, forming VGAM1010 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37330] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1010 folded precursor RNA into VGAM1010 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1010 RNA is designated SEQ ID:3721, and

is provided hereinbelow with reference to the sequence listing part.

[37331] VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1010 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37332] VGAM1010 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1010 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1010 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37333] The complementary binding of VGAM1010 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1010 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1010 host target RNA into VGAM1010 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37334] It is appreciated that VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1010 host target genes. The mRNA of each one of this plurality of VGAM1010 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1010 RNA, herein designated VGAM RNA, and which when bound by VGAM1010 RNA causes inhibition of translation of respective one or more VGAM1010 host target proteins.

[37335] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1010 gene, herein designated VGAM GENE, on one or more VGAM1010 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37336] It is yet further appreciated that a function of VGAM1010 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1010 correlate with, and may be deduced from, the identity of the host target genes which VGAM1010 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37337] Nucleotide sequences of the VGAM1010 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1010 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1010 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1010 are further described hereinbelow with reference to Table 1.

[37338] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1010 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1010 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37339] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1010 gene, herein designated VGAM is inhibition of expression of VGAM1010 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1010 correlate with, and may be deduced from, the identity of the target genes which VGAM1010 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37340] Cytokine Inducible SH2-containing Protein (CISH, Accession NM_013324) is a VGAM1010 host target gene. CISH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CISH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CISH BINDING SITE, designated SEQ ID:14971, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37341] A function of VGAM1010 is therefore inhibition of Cytokine Inducible SH2-containing Protein (CISH, Accession NM_013324), a gene which intervenes in the negative regulation of cytokines. Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CISH. The function

of CISH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM488. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326) is another VGAM1010 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14713, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37342] Another function of VGAM1010 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326), a gene which interact with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of MAPRE3 and its association with various diseases and clinical conditions, has been established by previous stud-

ies, as described hereinabove with reference to VGAM340.DKFZp434O0320 (Accession XM_097012) is another VGAM1010 host target gene. DKFZp434O0320 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp434O0320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0320 BINDING SITE, designated SEQ ID:40704, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37343] Another function of VGAM1010 is therefore inhibition of DKFZp434O0320 (Accession XM_097012). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0320. EPSIN (Accession NM_013333) is another VGAM1010 host target gene. EPSIN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EPSIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPSIN BIND-

ING SITE, designated SEQ ID:14980, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37344] Another function of VGAM1010 is therefore inhibition of EPSIN (Accession NM_013333). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPSIN. FASTK (Accession NM_025096) is another VGAM1010 host target gene. FASTK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FASTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FASTK BINDING SITE, designated SEQ ID:24728, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37345] Another function of VGAM1010 is therefore inhibition of FASTK (Accession NM_025096). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FASTK. HSPC065 (Accession NM_014157) is another VGAM1010 host target gene. HSPC065 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by HSPC065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15451, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37346] Another function of VGAM1010 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. MGC16025 (Accession NM_032923) is another VGAM1010 host target gene. MGC16025 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC16025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16025 BINDING SITE, designated SEQ ID:26748, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37347] Another function of VGAM1010 is therefore inhibition of

MGC16025 (Accession NM_032923). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16025. SEC8 (Accession NM_021807) is another VGAM1010 host target gene. SEC8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC8 BINDING SITE, designated SEQ ID:22360, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37348] Another function of VGAM1010 is therefore inhibition of SEC8 (Accession NM_021807). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC8. SYNE-2 (Accession NM_015180) is another VGAM1010 host target gene. SYNE-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNE-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SYNE-2 BINDING SITE, designated SEQ ID:17532, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37349] Another function of VGAM1010 is therefore inhibition of SYNE-2 (Accession NM_015180). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNE-2. Transducer of ERBB2, 2 (TOB2, Accession XM_170995) is another VGAM1010 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45767, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37350] Another function of VGAM1010 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM_170995). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC127435 (Accession

XM_072088) is another VGAM1010 host target gene.

LOC127435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127435 BINDING SITE, designated SEQ ID:37461, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37351] Another function of VGAM1010 is therefore inhibition of LOC127435 (Accession XM_072088). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127435. LOC157556 (Accession XM_098783) is another VGAM1010 host target gene. LOC157556 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157556 BINDING SITE, designated SEQ ID:41822, to the nucleotide sequence of VGAM1010 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3721.

[37352] Another function of VGAM1010 is therefore inhibition of LOC157556 (Accession XM_098783). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157556. LOC220143 (Accession XM_168046) is another VGAM1010 host target gene. LOC220143 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220143 BINDING SITE, designated SEQ ID:44952, to the nucleotide sequence of VGAM1010 RNA, herein designated VGAM RNA, also designated SEQ ID:3721.

[37353] Another function of VGAM1010 is therefore inhibition of LOC220143 (Accession XM_168046). Accordingly, utilities of VGAM1010 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220143. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1011 (VGAM1011) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37354] VGAM1011 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1011 was detected is described hereinabove with reference to Figs. 1–8.

[37355] VGAM1011 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37356] VGAM1011 gene encodes a VGAM1011 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1011 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1011 precursor RNA is designated SEQ ID:997, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:997 is located at position 29460 relative to the genome of Equine Herpesvirus 4.

[37357] VGAM1011 precursor RNA folds onto itself, forming

VGAM1011 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37358] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1011 folded precursor RNA into VGAM1011 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1011 RNA is designated SEQ ID:3722, and is provided hereinbelow with reference to the sequence listing part.

[37359] VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1011 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37360] VGAM1011 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1011 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1011 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37361] The complementary binding of VGAM1011 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1011 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1011 host target RNA into VGAM1011 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37362] It is appreciated that VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1011 host target genes. The mRNA of each one of this plurality of VGAM1011 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1011 RNA, herein designated VGAM RNA, and which when bound by VGAM1011 RNA causes inhibition of translation of respective one or more VGAM1011 host target proteins.

[37363] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1011 gene, herein designated VGAM GENE, on one or more VGAM1011 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37364] It is yet further appreciated that a function of VGAM1011 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1011 correlate with, and may be deduced from, the identity of the host target genes which VGAM1011 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[37365] Nucleotide sequences of the VGAM1011 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1011 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1011 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1011 are further described hereinbelow with reference to Table 1.

[37366] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1011 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1011 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37367] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1011 gene, herein designated VGAM is inhibition of expression of VGAM1011 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1011 correlate with, and may be deduced from, the identity of the target genes which VGAM1011 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[37368] Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM_000381) is a VGAM1011 host target gene. MID1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MID1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MID1 BINDING SITE, designated SEQ ID:5954, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37369] A function of VGAM1011 is therefore inhibition of Midline 1 (Opitz/BBB syndrome) (MID1, Accession NM_000381). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MID1. Mucin 3B (MUC3B, Accession XM_168578) is another VGAM1011 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ

ID:45253, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37370] Another function of VGAM1011 is therefore inhibition of Mucin 3B (MUC3B, Accession XM_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.V-myc Myelocytomatosis Viral Oncogene Homolog 1, Lung Carcinoma Derived (avian) (MYCL1, Accession NM_005376) is another VGAM1011 host target gene. MYCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCL1 BINDING SITE, designated SEQ ID:11852, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3722.

[37371] Another function of VGAM1011 is therefore inhibition of V-myc Myelocytomatosis Viral Oncogene Homolog 1, Lung Carcinoma Derived (avian) (MYCL1, Accession NM_005376), a gene which is a Myc-like transcription factor. Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCL1. The function of MYCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM640. T-cell Leukemia/lymphoma 1A (TCL1A, Accession NM_021966) is another VGAM1011 host target gene. TCL1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCL1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL1A BINDING SITE, designated SEQ ID:22498, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37372] Another function of VGAM1011 is therefore inhibition of T-cell Leukemia/lymphoma 1A (TCL1A, Accession

NM_021966). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL1A. Calpain 6 (CAPN6, Accession NM_014289) is another VGAM1011 host target gene. CAPN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN6 BINDING SITE, designated SEQ ID:15569, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37373] Another function of VGAM1011 is therefore inhibition of Calpain 6 (CAPN6, Accession NM_014289). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN6. FLJ11127 (Accession NM_019018) is another VGAM1011 host target gene. FLJ11127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of FLJ11127 BINDING SITE, designated SEQ ID:21108, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37374] Another function of VGAM1011 is therefore inhibition of FLJ11127 (Accession NM_019018). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11127. KIAA1971 (Accession XM_058720) is another VGAM1011 host target gene. KIAA1971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1971 BINDING SITE, designated SEQ ID:36726, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37375] Another function of VGAM1011 is therefore inhibition of KIAA1971 (Accession XM_058720). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1971. LOC146756 (Accession XM_097085) is another

VGAM1011 host target gene. LOC146756 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146756 BINDING SITE, designated SEQ ID:40733, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37376] Another function of VGAM1011 is therefore inhibition of LOC146756 (Accession XM_097085). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146756. LOC254015 (Accession XM_172977) is another VGAM1011 host target gene. LOC254015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254015 BINDING SITE, designated SEQ ID:46241, to the nucleotide sequence of VGAM1011 RNA, herein designated VGAM RNA, also designated SEQ ID:3722.

[37377] Another function of VGAM1011 is therefore inhibition of LOC254015 (Accession XM_172977). Accordingly, utilities of VGAM1011 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254015. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1012 (VGAM1012) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37378] VGAM1012 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1012 was detected is described hereinabove with reference to Figs. 1–8.

[37379] VGAM1012 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37380] VGAM1012 gene encodes a VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1012 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1012 precursor RNA is designated SEQ ID:998, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:998 is located at position 27830 relative to the genome of Equine Herpesvirus 1.

[37381] VGAM1012 precursor RNA folds onto itself, forming VGAM1012 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37382] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1012 folded precursor RNA into VGAM1012 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1012 RNA is designated SEQ ID:3723, and is provided hereinbelow with reference to the sequence listing part.

[37383] VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1012 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37384] VGAM1012 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1012 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1012 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37385] The complementary binding of VGAM1012 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1012 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1012 host target RNA into VGAM1012 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37386] It is appreciated that VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1012 host target genes. The mRNA of each one of this plurality of VGAM1012 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1012 RNA, herein designated VGAM RNA, and which when bound by VGAM1012 RNA causes inhibition of translation of respective one or more VGAM1012 host target proteins.

[37387] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1012 gene, herein designated VGAM GENE, on one or more VGAM1012 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37388] It is yet further appreciated that a function of VGAM1012 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1012 correlate with, and may be deduced from, the identity of the host target genes which VGAM1012 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37389] Nucleotide sequences of the VGAM1012 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1012 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1012 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1012 are further described hereinbelow with reference to Table 1.

[37390] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1012 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1012 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[37391] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1012 gene, herein designated VGAM is inhibition of expression of VGAM1012 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1012 correlate with, and may be deduced from, the identity of the target genes which VGAM1012 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37392] Collagen, Type XVIII, Alpha 1 (COL18A1, Accession NM_030582) is a VGAM1012 host target gene. COL18A1 BINDING SITE1 through COL18A1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL18A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL18A1 BINDING SITE1 through COL18A1 BINDING SITE3, designated SEQ ID:24955, SEQ ID:28206 and SEQ ID:28207 respectively, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37393] A function of VGAM1012 is therefore inhibition of Colla-

gen, Type XVIII, Alpha 1 (COL18A1, Accession NM_030582). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL18A1. EFS2 (Accession NM_005864) is another VGAM1012 host target gene. EFS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFS2 BINDING SITE, designated SEQ ID:12479, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37394] Another function of VGAM1012 is therefore inhibition of EFS2 (Accession NM_005864). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFS2. FLJ21032 (Accession NM_024906) is another VGAM1012 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24402, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37395] Another function of VGAM1012 is therefore inhibition of FLJ21032 (Accession NM_024906). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ23120 (Accession XM_097961) is another VGAM1012 host target gene. FLJ23120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23120 BINDING SITE, designated SEQ ID:41266, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37396] Another function of VGAM1012 is therefore inhibition of FLJ23120 (Accession XM_097961). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23120. KIAA0379 (Accession XM_042860) is another

VGAM1012 host target gene. KIAA0379 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0379, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0379 BINDING SITE, designated SEQ ID:33810, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37397] Another function of VGAM1012 is therefore inhibition of KIAA0379 (Accession XM_042860). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0379. LAP1B (Accession XM_035429) is another VGAM1012 host target gene. LAP1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAP1B BINDING SITE, designated SEQ ID:32263, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37398] Another function of VGAM1012 is therefore inhibition of LAP1B (Accession XM_035429). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAP1B. PBEF (Accession NM_005746) is another VGAM1012 host target gene. PBEF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PBEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PBEF BINDING SITE, designated SEQ ID:12307, to the nucleotide sequence of VGAM1012 RNA, herein designated VGAM RNA, also designated SEQ ID:3723.

[37399] Another function of VGAM1012 is therefore inhibition of PBEF (Accession NM_005746). Accordingly, utilities of VGAM1012 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PBEF. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1013 (VGAM1013) viral gene, which modulates expression of respective host target genes thereof, the function and

utility of which host target genes is known in the art.

[37400] VGAM1013 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1013 was detected is described hereinabove with reference to Figs. 1–8.

[37401] VGAM1013 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37402] VGAM1013 gene encodes a VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1013 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1013 precursor RNA is designated SEQ ID:999, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:999 is located at position 32583 relative to the genome of Equine Herpesvirus 1.

[37403] VGAM1013 precursor RNA folds onto itself, forming VGAM1013 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37404] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1013 folded precursor RNA into VGAM1013 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 86%) nucleotide sequence of VGAM1013 RNA is designated SEQ ID:3724, and is provided hereinbelow with reference to the sequence listing part.

[37405] VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1013 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[37406] VGAM1013 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1013 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1013 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[37407] The complementary binding of VGAM1013 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1013 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1013 host target RNA into VGAM1013 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37408] It is appreciated that VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1013 host target genes. The mRNA of each one of this plurality of VGAM1013 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1013 RNA, herein designated VGAM RNA, and which when bound by VGAM1013 RNA causes inhibition of translation of respective one or more VGAM1013 host target proteins.

[37409] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1013 gene, herein designated VGAM GENE, on one

or more VGAM1013 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37410] It is yet further appreciated that a function of VGAM1013 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1013 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1013 correlate with, and may be deduced from, the identity of the host target genes which VGAM1013 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37411] Nucleotide sequences of the VGAM1013 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1013 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1013 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1013 are further described hereinbelow with reference to Table 1.

[37412] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1013 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1013 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37413] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1013 gene, herein designated VGAM is inhibition of expression of VGAM1013 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1013 correlate with, and may be deduced from, the identity of the target genes which VGAM1013 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37414] DKFZP434O047 (Accession NM_015594) is a VGAM1013

host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17859, to the nucleotide sequence of VGAM1013 RNA, herein designated VGAM RNA, also designated SEQ ID:3724.

[37415] A function of VGAM1013 is therefore inhibition of DKFZP434O047 (Accession NM_015594). Accordingly, utilities of VGAM1013 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. FLJ32894 (Accession NM_144667) is another VGAM1013 host target gene. FLJ32894 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ32894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32894 BINDING SITE, designated SEQ ID:29484, to the nucleotide sequence of VGAM1013 RNA, herein designated VGAM RNA, also designated SEQ ID:3724.

[37416] Another function of VGAM1013 is therefore inhibition of FLJ32894 (Accession NM_144667). Accordingly, utilities of VGAM1013 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32894. LOC151248 (Accession XM_087143) is another VGAM1013 host target gene. LOC151248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151248 BINDING SITE, designated SEQ ID:39084, to the nucleotide sequence of VGAM1013 RNA, herein designated VGAM RNA, also designated SEQ ID:3724.

[37417] Another function of VGAM1013 is therefore inhibition of LOC151248 (Accession XM_087143). Accordingly, utilities of VGAM1013 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151248. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1014 (VGAM1014) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[37418] VGAM1014 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1014 was detected is described hereinabove with reference to Figs. 1–8.

[37419] VGAM1014 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37420] VGAM1014 gene encodes a VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1014 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1014 precursor RNA is designated SEQ ID:1000, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1000 is located at position 82653 relative to the genome of Rana Tigrina Ranavirus.

[37421] VGAM1014 precursor RNA folds onto itself, forming VGAM1014 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37422] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1014 folded precursor RNA into VGAM1014 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1014 RNA is designated SEQ ID:3725, and is provided hereinbelow with reference to the sequence listing part.

[37423] VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1014 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37424] VGAM1014 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1014 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1014 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37425] The complementary binding of VGAM1014 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1014 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1014 host target RNA into VGAM1014 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37426] It is appreciated that VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1014 host target genes. The mRNA of each one of this plurality of VGAM1014 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1014 RNA, herein designated VGAM RNA, and which when bound by VGAM1014 RNA causes inhibition of translation of respective one or more VGAM1014 host target proteins.

[37427] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1014 gene, herein designated VGAM GENE, on one or more VGAM1014 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37428] It is yet further appreciated that a function of VGAM1014 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1014 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1014 correlate with, and may be deduced from, the identity of the host target genes which VGAM1014 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[37429] Nucleotide sequences of the VGAM1014 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1014 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1014 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1014 are further described hereinbelow with reference to Table 1.

[37430] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1014 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1014 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37431] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1014 gene, herein designated VGAM is inhibition of expression of VGAM1014 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1014 correlate with, and may be deduced from, the identity of the target genes which VGAM1014 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37432] Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375) is a VGAM1014 host target gene.

C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33510, to the nucleotide sequence of VGAM1014 RNA, herein designated VGAM RNA, also designated SEQ ID:3725.

[37433] A function of VGAM1014 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375). Accordingly, utilities of VGAM1014 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. LOC196761 (Accession XM_116865) is another VGAM1014 host target gene. LOC196761 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196761 BINDING SITE, desig-

nated SEQ ID:43127, to the nucleotide sequence of VGAM1014 RNA, herein designated VGAM RNA, also designated SEQ ID:3725.

[37434] Another function of VGAM1014 is therefore inhibition of LOC196761 (Accession XM_116865). Accordingly, utilities of VGAM1014 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196761. LOC200609 (Accession XM_117256) is another VGAM1014 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43326, to the nucleotide sequence of VGAM1014 RNA, herein designated VGAM RNA, also designated SEQ ID:3725.

[37435] Another function of VGAM1014 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM1014 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1015 (VGAM1015) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37436] VGAM1015 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1015 was detected is described hereinabove with reference to Figs. 1–8.

[37437] VGAM1015 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Broad Bean Necrosis Virus. VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37438] VGAM1015 gene encodes a VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1015 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1015 precursor RNA is designated SEQ ID:1001, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1001 is located at position 1200 relative to the

genome of Broad Bean Necrosis Virus.

[37439] VGAM1015 precursor RNA folds onto itself, forming VGAM1015 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37440] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1015 folded precursor RNA into VGAM1015 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1015 RNA is designated SEQ ID:3726, and is provided hereinbelow with reference to the sequence listing part.

[37441] VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1015 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[37442] VGAM1015 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1015 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1015 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37443] The complementary binding of VGAM1015 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1015 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1015 host target RNA into VGAM1015 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37444] It is appreciated that VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1015 host target genes. The mRNA of each one of this plurality of VGAM1015 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1015 RNA, herein designated VGAM RNA, and which when bound by VGAM1015 RNA causes inhibition of translation of respective one or more VGAM1015 host target proteins.

[37445] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1015 gene, herein designated VGAM GENE, on one or more VGAM1015 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37446] It is yet further appreciated that a function of VGAM1015 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of viral infection by Broad Bean Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1015

correlate with, and may be deduced from, the identity of the host target genes which VGAM1015 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37447] Nucleotide sequences of the VGAM1015 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1015 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1015 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1015 are further described hereinbelow with reference to Table 1.

[37448] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1015 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1015 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37449] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1015 gene, herein designated VGAM is inhibition of expression of VGAM1015 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1015 correlate with, and may be deduced

from, the identity of the target genes which VGAM1015 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37450] Endothelin 2 (EDN2, Accession NM_001956) is a VGAM1015 host target gene. EDN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDN2 BINDING SITE, designated SEQ ID:7680, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37451] A function of VGAM1015 is therefore inhibition of Endothelin 2 (EDN2, Accession NM_001956), a gene which is a precursor of the hormone endothelin 2 which is an endothelium-derived vasoconstrictor peptide. Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDN2. The function of EDN2 has been established by previous studies. The human endothelins represent a gene family comprised of endothelin-1 (OMIM Ref. No. 131240), endothelin-2, and endothelin-3 (OMIM Ref. No.

131242). Based on the deduced amino acid sequences of the cloned ET2 and ET3 genes, corresponding proteins have been chemically synthesized and their vasoconstrictor activities studied. Of the 3 isopeptides, ET-2 has the most potent vasoconstrictor activity. Ohkubo et al. (1990) cloned cDNAs encoding human ET-2 precursor from a cDNA library constructed with mRNA derived from the human renal adenocarcinoma cell line, ACHN, which specifically secretes immunoreactive ET-2. The cDNA was found to contain 1.3 kb and to encode the preproprotein consisting of 178 amino acid residues. Northern blot analysis of mRNA suggested that the transcript was 1.4 kb. Bloch et al. (1991) used a cDNA clone for endothelin-2 to map the EDN2 gene to 1pter-p21 in human-mouse somatic cell hybrids. Southern blot hybridization demonstrated a single gene in both the human and the rat genome. Bloch et al. (1991) cloned the rat gene; the rat peptide differed from the human peptide at only 1 of 21 residues and was identical to mouse vasoactive intestinal contractor peptide (VIC). They concluded, therefore, that VIC is the mouse and rat analog of the human EDN2 gene. By Southern blot analysis of somatic cell hybrid DNAs and by in situ hybridization, Arinami et al. (1991) confirmed the assign-

ment of EDN2 to chromosome 1 and regionalized it to 1p34. Deng et al. (1994) found in the rat that the endothelin-2 gene is located on chromosome 5 and cosegregates strongly with systolic blood pressure in an F2 population derived from a cross of the Dahl salt-sensitive rat and the Lewis rat. Thus, ET2 is a quantitative trait locus (QTL) for blood pressure in the rat. ET1, ET3, and endothelin receptor type A (ETA; 131243) in the rat did not cosegregate with blood pressure in the several F2 populations tested.

[37452] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37453] Bloch, K. D.; Hong, C. C.; Eddy, R. L.; Shows, T. B.; Quert-ermous, T. : cDNA cloning and chromosomal assignment of the endothelin 2 gene: vasoactive intestinal contractor peptide is rat endothelin 2. *Genomics* 10: 236-242, 1991. ; and

[37454] Deng, A. Y.; Dene, H.; Pravenec, M.; Rapp, J. P. : Genetic mapping of two new blood pressure quantitative trait loci in the rat by genotyping endothelin system genes. *J. Clin. Invest.* 93.

[37455] Further studies establishing the function and utilities of

EDN2 are found in John Hopkins OMIM database record ID 131241, and in cited publications numbered 12211–2289 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749) is another VGAM1015 host target gene. SLC20A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC20A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC20A2 BINDING SITE, designated SEQ ID:13602, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37456] Another function of VGAM1015 is therefore inhibition of Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749), a gene which is a sodium–phosphate symporter. Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC20A2. The function of SLC20A2 and its association with various diseases and clinical conditions, has been es–

established by previous studies, as described hereinabove with reference to VGAM232.FLJ13231 (Accession NM_023073) is another VGAM1015 host target gene. FLJ13231 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13231 BINDING SITE, designated SEQ ID:23329, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37457] Another function of VGAM1015 is therefore inhibition of FLJ13231 (Accession NM_023073). Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13231. KIAA0981 (Accession XM_028867) is another VGAM1015 host target gene. KIAA0981 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0981 BINDING SITE, designated SEQ ID:30795, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37458] Another function of VGAM1015 is therefore inhibition of KIAA0981 (Accession XM_028867). Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0981. LOC148014 (Accession XM_085999) is another VGAM1015 host target gene. LOC148014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148014 BINDING SITE, designated SEQ ID:38441, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37459] Another function of VGAM1015 is therefore inhibition of LOC148014 (Accession XM_085999). Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148014. LOC152627 (Accession XM_087495) is another VGAM1015 host target gene. LOC152627 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39292, to the nucleotide sequence of VGAM1015 RNA, herein designated VGAM RNA, also designated SEQ ID:3726.

[37460] Another function of VGAM1015 is therefore inhibition of LOC152627 (Accession XM_087495). Accordingly, utilities of VGAM1015 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152627. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1016 (VGAM1016) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37461] VGAM1016 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1016 was detected is described hereinabove with reference to Figs. 1-8.

[37462] VGAM1016 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Broad Bean Necrosis Virus. VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37463] VGAM1016 gene encodes a VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1016 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1016 precursor RNA is designated SEQ ID:1002, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1002 is located at position 4420 relative to the genome of Broad Bean Necrosis Virus.

[37464] VGAM1016 precursor RNA folds onto itself, forming VGAM1016 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[37465] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1016 folded precursor RNA into VGAM1016 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1016 RNA is designated SEQ ID:3727, and is provided hereinbelow with reference to the sequence listing part.

[37466] VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1016 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37467] VGAM1016 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1016 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1016 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1016 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37468] The complementary binding of VGAM1016 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1016 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1016 host target RNA into VGAM1016 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37469] It is appreciated that VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1016 host target genes. The mRNA of each one of this plurality of VGAM1016 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1016 RNA, herein designated VGAM RNA, and which when bound by VGAM1016 RNA causes inhibition of translation of respective one or more VGAM1016 host target proteins.

[37470] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1016 gene, herein designated VGAM GENE, on one or more VGAM1016 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37471] It is yet further appreciated that a function of VGAM1016 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of viral infection by Broad Bean Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1016 correlate with, and may be deduced from, the identity of the host target genes which VGAM1016 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37472] Nucleotide sequences of the VGAM1016 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1016 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1016 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1016 are further described hereinbelow with reference to Table 1.

[37473] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1016 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1016 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37474] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1016 gene, herein designated VGAM is inhibition of expression of VGAM1016 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1016 correlate with, and may be deduced from, the identity of the target genes which VGAM1016 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37475] S-adenosylmethionine Decarboxylase 1 (AMD1, Accession NM_001634) is a VGAM1016 host target gene. AMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of AMD1 BINDING SITE, designated SEQ ID:7348, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37476] A function of VGAM1016 is therefore inhibition of S-adenosylmethionine Decarboxylase 1 (AMD1, Accession NM_001634), a gene which catalyzes the removal of the carboxylate group of S-adenosylmethionine in the polyamine biosynthesis pathway. Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMD1. The function of AMD1 has been established by previous studies. The polyamines spermine, spermidine, and putrescine are low molecular weight aliphatic amines essential for cellular proliferation and tumor promotion. Ornithine decarboxylase (ODC; 165640) and S-adenosylmethionine decarboxylase (AdoMetDC) catalyze the rate-limiting steps in polyamine biosynthesis. A concordant rise in ODC and AdoMetDC activity is seen in various neoplastic conditions including colon cancer and benign colonic polyps. A rat cDNA clone for AdoMetDC was used by Radford et al. (1987, 1989) in mouse-human somatic cell hybrid experiments to map the AMD gene to

chromosomes 6 and X. They demonstrated that the gene on chromosome 6, symbolized AMD1, is not amplified in colon neoplasia. The sequence on X, symbolized AMD2, was localized to Xq22–q28 and may represent a pseudogene. That AMD2 is indeed a pseudogene was indicated by the findings of Maric et al. (1992) that the X-chromosome gene lacks introns which are present in the chromosome 6 gene. The gene on chromosome 6 encompasses at least 22 kb and comprises 9 exons and 8 introns, in contrast to the corresponding rat gene that has only 8 exons. Other aspects of the structure and organization were presented by Maric et al. (1992). Pulkka et al. (1993) characterized 2 AMD genes in the rat and localized both to rat chromosome 20 by mouse–rat somatic cell hybrids. They showed a high degree of conservation of sequence and structural organization in the coding portions but the 5–prime flanking regions were totally different. Maric et al. (1995) characterized the AMD pseudogene on the X chromosome. It lacks all the introns present in AMD1 and has numerous mutations in the protein–coding region. By fluorescence in situ hybridization, they mapped AMD1 to 6q21–q22 and the pseudogene, which they referred to as AMD2, to Xq28.

[37477] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37478] Maric, S. C.; Crozat, A.; Janne, O. A. : Structure and organization of the human S-adenosylmethionine decarboxylase gene. J. Biol. Chem. 267: 18915–18923, 1992. ; and

[37479] Maric, S. C.; Crozat, A.; Louhimo, J.; Knuutila, S.; Janne, O. A. : The human S-adenosylmethionine decarboxylase gene: nucleotide sequence of a pseudogene and chromosomal localization o.

[37480] Further studies establishing the function and utilities of AMD1 are found in John Hopkins OMIM database record ID 180980, and in cited publications numbered 11117–11118, 10267–1026 and 44 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphatidylinositol Transfer Protein, Beta (PITPNB, Accession NM_012399) is another VGAM1016 host target gene. PITPNB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PITPNB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PITPNB BIND-

ING SITE, designated SEQ ID:14764, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37481] Another function of VGAM1016 is therefore inhibition of Phosphatidylinositol Transfer Protein, Beta (PITPNB, Accession NM_012399), a gene which catalyzes the transfer of ptdins and phosphatidylcholine between membranes. Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PITPNB. The function of PITPNB has been established by previous studies. Tanaka et al. (1995) cloned PITPNB cDNA by screening a human brain cDNA library with the rat brain cDNA homolog as probe. The deduced 271-amino acid protein has a calculated molecular mass of 31.5 kD and shows 98.1% sequence identity with the rat protein. Northern blot analysis detected ubiquitous expression of a 3.4-kb transcript, with highest expression in liver and lowest in skeletal muscle. Expression was found in all regions of the brain examined, with highest expression in amygdala. Phosphatidylinositol transfer protein is a member of a diverse set of cytosolic phospholipid transfer proteins that are distinguished by their ability to transfer phospholipids between membranes in vitro

(Wirtz, 1991).

[37482] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37483] Tanaka, S.; Yamashita, S.; Hosaka, K. : Cloning and expression of human cDNA encoding phosphatidylinositol transfer protein beta. *Biochim. Biophys. Acta* 1259: 199–202, 1995. ; and

[37484] Wirtz, K. W. A. : Phospholipid transfer proteins. *Annu. Rev. Biochem.* 60: 73–99, 1991.

[37485] Further studies establishing the function and utilities of PITPNB are found in John Hopkins OMIM database record ID 606876, and in cited publications numbered 608 and 8227 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinitis Pigmentosa 2 (X-linked recessive) (RP2, Accession NM_006915) is another VGAM1016 host target gene. RP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP2 BINDING SITE, designated SEQ ID:13791, to the nu-

cleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37486] Another function of VGAM1016 is therefore inhibition of Retinitis Pigmentosa 2 (X-linked recessive) (RP2, Accession NM_006915). Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP2. Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723) is another VGAM1016 host target gene. ARHGEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF2 BINDING SITE, designated SEQ ID:11089, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37487] Another function of VGAM1016 is therefore inhibition of Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723). Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

ARHGEF2. CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM_013354) is another VGAM1016 host target gene. CNOT7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNOT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT7 BINDING SITE, designated SEQ ID:14999, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37488] Another function of VGAM1016 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM_013354). Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT7. LOC163341 (Accession XM_088817) is another VGAM1016 host target gene. LOC163341 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC163341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC163341 BINDING SITE, designated SEQ ID:39948, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37489] Another function of VGAM1016 is therefore inhibition of LOC163341 (Accession XM_088817). Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163341. LOC219920 (Accession XM_167787) is another VGAM1016 host target gene. LOC219920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219920 BINDING SITE, designated SEQ ID:44811, to the nucleotide sequence of VGAM1016 RNA, herein designated VGAM RNA, also designated SEQ ID:3727.

[37490] Another function of VGAM1016 is therefore inhibition of LOC219920 (Accession XM_167787). Accordingly, utilities of VGAM1016 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219920. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1017 (VGAM1017) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37491] VGAM1017 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1017 was detected is described hereinabove with reference to Figs. 1–8.

[37492] VGAM1017 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Western Yellows Virus. VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37493] VGAM1017 gene encodes a VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1017 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1017 precursor RNA is designated SEQ ID:1003, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1003 is located at position 4604 relative to the

genome of Beet Western Yellows Virus.

[37494] VGAM1017 precursor RNA folds onto itself, forming VGAM1017 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37495] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1017 folded precursor RNA into VGAM1017 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1017 RNA is designated SEQ ID:3728, and is provided hereinbelow with reference to the sequence listing part.

[37496] VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1017 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[37497] VGAM1017 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1017 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1017 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[37498] The complementary binding of VGAM1017 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1017 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1017 host target RNA into VGAM1017 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37499] It is appreciated that VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1017 host target genes. The mRNA of each one of this plurality of VGAM1017 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1017 RNA, herein designated VGAM RNA, and which when bound by VGAM1017 RNA causes inhibition of translation of respective one or more VGAM1017 host target proteins.

[37500] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1017 gene, herein designated VGAM GENE, on one or more VGAM1017 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37501] It is yet further appreciated that a function of VGAM1017 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of viral infection by Beet Western Yellows Virus. Specific functions, and accordingly utilities, of VGAM1017

correlate with, and may be deduced from, the identity of the host target genes which VGAM1017 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37502] Nucleotide sequences of the VGAM1017 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1017 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1017 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1017 are further described hereinbelow with reference to Table 1.

[37503] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1017 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1017 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37504] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1017 gene, herein designated VGAM is inhibition of expression of VGAM1017 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1017 correlate with, and may be deduced

from, the identity of the target genes which VGAM1017 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37505] Kinesin Family Member 3B (KIF3B, Accession NM_004798) is a VGAM1017 host target gene. KIF3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3B BINDING SITE, designated SEQ ID:11215, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37506] A function of VGAM1017 is therefore inhibition of Kinesin Family Member 3B (KIF3B, Accession NM_004798), a gene which is a microtubule-based anterograde translocator for membranous organelles. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF3B. The function of KIF3B has been established by previous studies. In eukaryotic cells, proteins and lipids are sorted and transported to their correct destinations at distinct velocities by each organelle or protein complex. Kinesin

superfamily proteins are a molecular motor superfamily involved in these processes, conveying their own cargoes along microtubules. Nagase et al. (1997) cloned the KIF3B gene, which they referred to as KIAA0359, the human homolog of the mouse kinase superfamily 3B gene (Yamazaki et al., 1995). The human KIF3B gene encodes a 747-amino acid protein that shares 98% identity with the mouse Kif3b protein. RT-PCR analysis revealed that the KIF3B gene was ubiquitously expressed in all human tissues tested. By analysis of radiation hybrid panels, Nagase et al. (1997) mapped the KIF3B gene to chromosome 20. Animal model experiments lend further support to the function of KIF3B. By gene targeting, Nonaka et al. (1998) disrupted the murine Kif3b gene. The null mutants did not survive beyond midgestation, exhibiting growth retardation, pericardial sac ballooning, and neural tube disorganization. Prominently, the left-right asymmetry was randomized in the heart loop and the direction of embryonic turning. Lefty-2 (OMIM Ref. No. 603037) expression was either bilateral or absent. Furthermore, the node lacked monocilia while the basal bodies were present. Immunocytochemistry revealed Kif3b localization in wildtype nodal cilia. Video microscopy showed that these cilia were

motile and generated a leftward flow. These data suggested that KIF3B is essential for the left-right determination through intraciliary transportation of materials for ciliogenesis of motile primary cilia that could produce a gradient of putative morphogen along the left-right axis in the node

[37507] It is appreciated that the abovementioned animal model for KIF3B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[37508] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37509] Nagase, T.; Ishikawa, K.; Nakajima, D.; Ohira, M.; Seki, N.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 4: 141–150, 1997. ; and

[37510] Nonaka, S.; Tanaka, Y.; Okada, Y.; Takeda, S.; Harada, A.; Kanai, Y.; Kido, M.; Hirokawa, N. : Randomization of left-right asymmetry due to loss of nodal cilia generating leftward flow.

[37511] Further studies establishing the function and utilities of KIF3B are found in John Hopkins OMIM database record ID 603754, and in cited publications numbered 95 and 7600–7601 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lactate Dehydrogenase B (LDHB, Accession NM_002300) is another VGAM1017 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8086, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37512] Another function of VGAM1017 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM273.Neural Precursor Cell Expressed, Developmentally Down-regulated 4-like (NEDD4L, Accession NM_015277) is another VGAM1017 host target gene. NEDD4L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEDD4L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEDD4L BINDING SITE, designated SEQ ID:17605, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37513] Another function of VGAM1017 is therefore inhibition of Neural Precursor Cell Expressed, Developmentally Down-regulated 4-like (NEDD4L, Accession NM_015277), a gene which may play a role in the regulation of epithelial sodium channel function. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEDD4L. The function of NEDD4L and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM603.Protein Phosphatase 1, Regulatory

(inhibitor) Subunit 3C (PPP1R3C, Accession NM_005398) is another VGAM1017 host target gene. PPP1R3C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3C BINDING SITE, designated SEQ ID:11877, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37514] Another function of VGAM1017 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3C (PPP1R3C, Accession NM_005398). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3C. Regulatory Factor X-associated Protein (RFXAP, Accession NM_000538) is another VGAM1017 host target gene. RFXAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFXAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFXAP BINDING SITE, designated SEQ

ID:6137, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37515] Another function of VGAM1017 is therefore inhibition of Regulatory Factor X-associated Protein (RFXAP, Accession NM_000538), a gene which binds to the x-box of mhc ii promoters and is a transcriptional regulator. Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFXAP. The function of RFXAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM797. Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083) is another VGAM1017 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22054, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37516] Another function of VGAM1017 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665) is another VGAM1017 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12206, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37517] Another function of VGAM1017 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. IMAGE145052 (Accession NM_014267) is another VGAM1017 host target gene. IMAGE145052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA en-

coded by IMAGE145052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMAGE145052 BINDING SITE, designated SEQ ID:15542, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37518] Another function of VGAM1017 is therefore inhibition of IMAGE145052 (Accession NM_014267). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMAGE145052. KIAA0040 (Accession NM_014656) is another VGAM1017 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16093, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37519] Another function of VGAM1017 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities

of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. KIAA0410 (Accession NM_014778) is another VGAM1017 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16613, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37520] Another function of VGAM1017 is therefore inhibition of KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0410. KIAA1579 (Accession NM_018211) is another VGAM1017 host target gene. KIAA1579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1579 BINDING SITE, designated SEQ ID:20117, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37521] Another function of VGAM1017 is therefore inhibition of KIAA1579 (Accession NM_018211). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1579. MGC10999 (Accession NM_032307) is another VGAM1017 host target gene. MGC10999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10999 BINDING SITE, designated SEQ ID:26088, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37522] Another function of VGAM1017 is therefore inhibition of MGC10999 (Accession NM_032307). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10999. Nei Like 2 (E. coli) (NEIL2, Accession NM_145043) is another VGAM1017 host target gene.

NEIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEIL2 BINDING SITE, designated SEQ ID:29674, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37523] Another function of VGAM1017 is therefore inhibition of Nei Like 2 (E. coli) (NEIL2, Accession NM_145043). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEIL2. SSH2 (Accession XM_030846) is another VGAM1017 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31174, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37524] Another function of VGAM1017 is therefore inhibition of

SSH2 (Accession XM_030846). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. LOC126302 (Accession XM_059020) is another VGAM1017 host target gene. LOC126302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126302 BINDING SITE, designated SEQ ID:36818, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37525] Another function of VGAM1017 is therefore inhibition of LOC126302 (Accession XM_059020). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126302. LOC145463 (Accession XM_048173) is another VGAM1017 host target gene. LOC145463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC145463 BINDING SITE, designated SEQ ID:35121, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37526] Another function of VGAM1017 is therefore inhibition of LOC145463 (Accession XM_048173). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145463. LOC255082 (Accession XM_172843) is another VGAM1017 host target gene. LOC255082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255082 BINDING SITE, designated SEQ ID:46117, to the nucleotide sequence of VGAM1017 RNA, herein designated VGAM RNA, also designated SEQ ID:3728.

[37527] Another function of VGAM1017 is therefore inhibition of LOC255082 (Accession XM_172843). Accordingly, utilities of VGAM1017 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255082. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1018 (VGAM1018) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37528] VGAM1018 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1018 was detected is described hereinabove with reference to Figs. 1–8.

[37529] VGAM1018 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Western Yellows Virus. VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37530] VGAM1018 gene encodes a VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1018 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1018 precursor RNA is designated SEQ ID:1004, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1004 is located at position 3512 relative to the genome of Beet Western Yellows Virus.

[37531] VGAM1018 precursor RNA folds onto itself, forming VGAM1018 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37532] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1018 folded precursor RNA into VGAM1018 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1018 RNA is designated SEQ ID:3729, and is provided hereinbelow with reference to the sequence listing part.

[37533] VGAM1018 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1018 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37534] VGAM1018 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1018 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1018 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1018 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[37535] The complementary binding of VGAM1018 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1018 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1018 host target RNA into VGAM1018 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37536] It is appreciated that VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1018 host target genes. The mRNA of each one of this plurality of VGAM1018 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1018 RNA, herein designated VGAM RNA, and which when bound by VGAM1018 RNA causes inhibition of translation of respective one or more

VGAM1018 host target proteins.

[37537] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1018 gene, herein designated VGAM GENE, on one or more VGAM1018 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37538] It is yet further appreciated that a function of VGAM1018 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1018 include diagnosis, prevention and treatment of viral infection by Beet Western Yellows Virus.

Specific functions, and accordingly utilities, of VGAM1018 correlate with, and may be deduced from, the identity of the host target genes which VGAM1018 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37539] Nucleotide sequences of the VGAM1018 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1018 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1018 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1018 are further described hereinbelow with reference to Table 1.

[37540] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1018 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1018 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37541] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1018 gene, herein designated VGAM is inhibition of expression of VGAM1018 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1018 correlate with, and may be deduced from, the identity of the target genes which VGAM1018 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37542] KIAA0556 (Accession XM_044632) is a VGAM1018 host target gene. KIAA0556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0556 BINDING SITE, designated SEQ ID:34247, to the nucleotide sequence of VGAM1018 RNA, herein designated VGAM RNA, also designated SEQ ID:3729.

[37543] A function of VGAM1018 is therefore inhibition of KIAA0556 (Accession XM_044632). Accordingly, utilities of VGAM1018 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0556. LOC256052 (Accession XM_174732) is another VGAM1018 host target gene. LOC256052 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256052, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256052 BINDING SITE, designated SEQ ID:46603, to the nucleotide sequence of VGAM1018 RNA, herein designated VGAM RNA, also designated SEQ ID:3729.

[37544] Another function of VGAM1018 is therefore inhibition of LOC256052 (Accession XM_174732). Accordingly, utilities of VGAM1018 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256052. LOC90139 (Accession NM_130783) is another VGAM1018 host target gene. LOC90139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90139 BINDING SITE, designated SEQ ID:28272, to the nucleotide sequence of VGAM1018 RNA, herein designated VGAM RNA, also designated SEQ ID:3729.

[37545] Another function of VGAM1018 is therefore inhibition of LOC90139 (Accession NM_130783). Accordingly, utilities of VGAM1018 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90139. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1019 (VGAM1019) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37546] VGAM1019 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1019 was detected is described hereinabove with reference to Figs. 1–8.

[37547] VGAM1019 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Western Yellows Virus. VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37548] VGAM1019 gene encodes a VGAM1019 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1019 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1019 precursor RNA is designated SEQ ID:1005, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1005 is located at position 5178 relative to the genome of Beet Western Yellows Virus.

- [37549] VGAM1019 precursor RNA folds onto itself, forming VGAM1019 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [37550] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1019 folded precursor RNA into VGAM1019 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1019 RNA is designated SEQ ID:3730, and is provided hereinbelow with reference to the sequence listing part.

[37551] VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1019 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37552] VGAM1019 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1019 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1019 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37553] The complementary binding of VGAM1019 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1019 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1019 host target RNA into VGAM1019 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37554] It is appreciated that VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1019 host target genes. The mRNA of each one of this plurality of VGAM1019 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1019 RNA, herein designated VGAM RNA, and which when bound by VGAM1019 RNA causes

inhibition of translation of respective one or more VGAM1019 host target proteins.

[37555] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1019 gene, herein designated VGAM GENE, on one or more VGAM1019 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37556] It is yet further appreciated that a function of VGAM1019 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1019 include diagnosis, prevention and

treatment of viral infection by Beet Western Yellows Virus. Specific functions, and accordingly utilities, of VGAM1019 correlate with, and may be deduced from, the identity of the host target genes which VGAM1019 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37557] Nucleotide sequences of the VGAM1019 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1019 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1019 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1019 are further described hereinbelow with reference to Table 1.

[37558] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1019 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1019 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37559] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1019 gene, herein designated VGAM is inhibition of expression of VGAM1019 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1019 correlate with, and may be deduced from, the identity of the target genes which VGAM1019 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37560] Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774) is a VGAM1019 host target gene. ANK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE, designated SEQ ID:30290, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37561] A function of VGAM1019 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. EphB6 (EPHB6, Accession NM_004445) is another VGAM1019 host target gene. EPHB6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EPHB6, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB6 BINDING SITE, designated SEQ ID:10740, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37562] Another function of VGAM1019 is therefore inhibition of EphB6 (EPHB6, Accession NM_004445), a gene which Putative Eph-related receptor tyrosine kinase B6. Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB6. The function of EPHB6 has been established by previous studies. See 179610 for background on Eph receptors and their ligands, the ephrins. By screening human brain and hematopoietic cell cDNA libraries with the catalytic domain of EPHB4 (OMIM Ref. No. 600011), Matsuoka et al. (1997) cloned a cDNA encoding EPHB6. The predicted 1,006-amino acid EPHB6 protein has the primary structural features of Eph-family receptor tyrosine kinases, but it lacks several invariant residues that have been shown to be essential for tyrosine kinase activity. Expression of the catalytic domain of EPHB6 in mammalian cells resulted in no detectable tyrosine kinase ac-

tivity in an in vitro assay. Northern blot analysis of normal human adult tissues showed that EPHB6 was expressed as a single 4.0-kb transcript in all tissues examined, with very strong expression in the brain and pancreas. EPHB6 is expressed in normal human brain as a 135-kD protein. By fluorescence in situ hybridization, Matsuoka et al. (1997) mapped the EPHB6 gene to 7q33–q35. Neuroblastoma (NB; 256700) is a common pediatric tumor that exhibits a wide range of biologic and clinical heterogeneity. EPH family receptor tyrosine kinases and ligand ephrins play pivotal roles in neural and cardiovascular development. High-level expression of transcripts encoding EPHB6 and its ligands ephrin-B2 (EFNB2; 600527) and ephrin-B3 (EFNB3; 602297) is associated with low-stage NB (stages 1, 2, and 4S) and high expression of TRKA (NTRK1; 191315). Tang et al. (2000) showed that EFNB2 and TRKA expressions were associated with both tumor stage and patient age, whereas EPHB6 and EFNB3 expressions were solely associated with tumor stage, suggesting that these genes were expressed in different subsets of NB. High-level expression of EPHB6, EFNB2, and EFNB3 predicted favorable NB outcome, and their expression combined with TRKA expression predicted the disease

outcome more accurately than each variable alone. If any 1 of the 4 genes was expressed at high levels in NB, the patient survival was excellent (more than 90%). Tang et al. (2000) found that transfection of EPHB6 cDNA into neuroblastoma cell lines expressing little endogenous EPHB6 resulted in inhibition of their clonogenicity in culture. Furthermore, transfection of EPHB6 suppressed the tumorigenicity of a cell line in a mouse xenograft model, demonstrating that high-level expressions of favorable NB genes, such as EPHB6, can in fact suppress malignant phenotype of unfavorable NB.

[37563] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37564] Matsuoka, H.; Iwata, N.; Ito, M.; Shimoyama, M.; Nagata, A.; Chihara, K.; Takai, S.; Matsui, T. : Expression of a kinase-defective Eph-like receptor in the normal human brain. *Biochem. Biophys. Res. Commun.* 235: 487-492, 1997. ; and

[37565] Tang, X. X.; Zhao, H.; Robinson, M. E.; Cohen, B.; Cnaan, A.; London, W.; Cohn, S. L.; Cheung, N.-K. V.; Brodeur, G. M.; Evans, A. E.; Ikegaki, N. : Implications of EPHB6, EFNB2, and EFN.

[37566] Further studies establishing the function and utilities of EPHB6 are found in John Hopkins OMIM database record ID 602757, and in cited publications numbered 5887–5888 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Erbb2 Interacting Protein (ERBB2IP, Accession NM_018695) is another VGAM1019 host target gene. ERBB2IP BINDING SITE1 and ERBB2IP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ERBB2IP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERBB2IP BINDING SITE1 and ERBB2IP BINDING SITE2, designated SEQ ID:20771 and SEQ ID:20772 respectively, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37567] Another function of VGAM1019 is therefore inhibition of Erbb2 Interacting Protein (ERBB2IP, Accession NM_018695), a gene which ERBB2 interacting protein; acts as an adaptor for the receptor ERBB2/HER2. Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ERBB2IP. The function of ERBB2IP has been established by previous studies. In a yeast 2-hybrid screen of a mouse kidney cDNA library with the 9 C-terminal residues of ErbB2 (OMIM Ref. No. 164870) as bait, Borg et al. (2000) cloned ErbB2ip, which they called Erbin. They cloned human ERBB2IP by RT-PCR of a human B-lymphocyte cell line. The deduced 1,371-amino acid protein contains 16 canonical LRR (leucine-rich repeat) motifs at the N terminus, followed by an LRR-like domain, proline-rich stretches that may represent binding sites for SH3 and WW domains, and a C-terminal PDZ domain. Northern blot analysis revealed a 7.2-kb transcript in most human and mouse tissues. Western blot analysis indicated a 180-kD doublet in all tissues tested. Favre et al. (2001) cloned ERBB2IP in a yeast 2-hybrid screen of a human keratinocyte cDNA library with the N terminus of bullous pemphigoid antigen-1 (BPAG1; 113810) as bait. They observed several splice variants. ERBB2IP was expressed as a doublet of about 6.9 to 7.4 kb in human keratinocytes and in a keratinocyte cell line. Semiquantitative RT-PCR indicated numerous transcripts expressed in most tissues. Western blot analysis showed a 200-kD in differentiated cells but not in undifferentiated keratinocytes.

Huang et al. (2001) cloned Erbb2ip from mouse muscle, brain, and heart cDNA libraries in a yeast 2-hybrid screen using Erbb2 as bait. Erbb2ip was expressed as a 180-kD protein in brain, skeletal muscle, primary muscle cultures, and muscle cell lines. Erbb2ip expression was found at a similar level in myoblasts and myotubes, suggesting that expression is not differentially regulated in muscle. By immunolocalization studies, they colocalized Erbb2ip with the acetylcholine receptor at the neuromuscular junction. Both Erbb2 and Erbb2ip were also found in synaptosomes from adult mouse brain and copurified with postsynaptic densities. The International Radiation Hybrid Mapping Consortium mapped the ERBB2IP gene to chromosome 5 (WI-31186). Favre et al. (2001) stated that sequence analysis places the ERBB2IP gene on the long arm of chromosome 5 between D5S427 and D5S647.

[37568] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37569] Favre, B.; Fontao, L.; Koster, J.; Shafaatian, R.; Jaunin, F.; Saurat, J.-H.; Sonnenberg, A.; Borradori, L. : The hemidesmosomal protein bullous pemphigoid antigen 1 and the integrin beta-4 subunit bind to ERBIN: molecular

cloning of multiple alternative splice variants of ERBIN and analysis of their tissue expression. J. Biol. Chem. 276: 32427–32436, 2001. ; and

[37570] Huang, Y. Z.; Wang, Q.; Xiong, W. C.; Mei, L. : Erbin is a protein concentrated at postsynaptic membranes that interacts with PSD-95. J. Biol. Chem. 276: 19318–19326, 2001.

[37571] Further studies establishing the function and utilities of ERBB2IP are found in John Hopkins OMIM database record ID 606944, and in cited publications numbered 527 and 5367 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_014001) is another VGAM1019 host target gene. GGA3 BINDING SITE1 and GGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA3 BINDING SITE1 and GGA3 BINDING SITE2, designated SEQ ID:15198 and SEQ ID:42262 respectively, to the nucleotide sequence of VGAM1019 RNA, herein designated

VGAM RNA, also designated SEQ ID:3730.

[37572] Another function of VGAM1019 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_014001), a gene which may play a role in the regulation of membrane traffic through the trans-golgi network. Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA3. The function of GGA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM353. BART1 (Accession NM_012106) is another VGAM1019 host target gene. BART1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BART1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BART1 BINDING SITE, designated SEQ ID:14424, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37573] Another function of VGAM1019 is therefore inhibition of BART1 (Accession NM_012106). Accordingly, utilities of

VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BART1. Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943) is another VGAM1019 host target gene. CLIC4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLIC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC4 BINDING SITE, designated SEQ ID:15130, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37574] Another function of VGAM1019 is therefore inhibition of Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC4. CMG2 (Accession NM_058172) is another VGAM1019 host target gene. CMG2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CMG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of CMG2 BINDING SITE, designated SEQ ID:27721, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37575] Another function of VGAM1019 is therefore inhibition of CMG2 (Accession NM_058172). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMG2. DKFZp761K1423 (Accession NM_018422) is another VGAM1019 host target gene. DKFZp761K1423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761K1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761K1423 BINDING SITE, designated SEQ ID:20472, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37576] Another function of VGAM1019 is therefore inhibition of DKFZp761K1423 (Accession NM_018422). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp761K1423. GAPCENA (Accession NM_012197) is another VGAM1019 host target gene. GAPCENA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GAPCENA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAPCENA BINDING SITE, designated SEQ ID:14493, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37577] Another function of VGAM1019 is therefore inhibition of GAPCENA (Accession NM_012197). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAPCENA. G Protein Pathway Suppressor 2 (GPS2, Accession XM_102749) is another VGAM1019 host target gene. GPS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPS2 BINDING SITE, designated SEQ ID:42145, to the nucleotide sequence of VGAM1019 RNA, herein designated

VGAM RNA, also designated SEQ ID:3730.

[37578] Another function of VGAM1019 is therefore inhibition of G Protein Pathway Suppressor 2 (GPS2, Accession XM_102749). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPS2. HTEX4 (Accession XM_166378) is another VGAM1019 host target gene. HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HTEX4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTEX4 BINDING SITE1 through HTEX4 BINDING SITE3, designated SEQ ID:44216, SEQ ID:46652 and SEQ ID:46721 respectively, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37579] Another function of VGAM1019 is therefore inhibition of HTEX4 (Accession XM_166378). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTEX4. KIAA1887 (Accession XM_084801) is another VGAM1019 host target gene. KIAA1887 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by KIAA1887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1887 BINDING SITE, designated SEQ ID:37716, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37580] Another function of VGAM1019 is therefore inhibition of KIAA1887 (Accession XM_084801). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1887. MGC13061 (Accession NM_032322) is another VGAM1019 host target gene. MGC13061 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC13061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13061 BINDING SITE, designated SEQ ID:26128, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37581] Another function of VGAM1019 is therefore inhibition of

MGC13061 (Accession NM_032322). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13061. Phospholipid Scramblase 2 (PLSCR2, Accession NM_020359) is another VGAM1019 host target gene. PLSCR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLSCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR2 BINDING SITE, designated SEQ ID:21630, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37582] Another function of VGAM1019 is therefore inhibition of Phospholipid Scramblase 2 (PLSCR2, Accession NM_020359). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR2. Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_138727) is another VGAM1019 host target gene. ST7L BINDING SITE1 through ST7L BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

ST7L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7L BINDING SITE1 through ST7L BINDING SITE3, designated SEQ ID:28975, SEQ ID:29205 and SEQ ID:19333 respectively, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37583] Another function of VGAM1019 is therefore inhibition of Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_138727). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7L. Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037) is another VGAM1019 host target gene. TNRC9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNRC9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC9 BINDING SITE, designated SEQ ID:35320, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37584] Another function of VGAM1019 is therefore inhibition of Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC9. LOC120534 (Accession XM_058476) is another VGAM1019 host target gene. LOC120534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120534 BINDING SITE, designated SEQ ID:36625, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37585] Another function of VGAM1019 is therefore inhibition of LOC120534 (Accession XM_058476). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120534. LOC147991 (Accession XM_085993) is another VGAM1019 host target gene. LOC147991 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147991, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147991 BINDING SITE, designated SEQ ID:38434, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37586] Another function of VGAM1019 is therefore inhibition of LOC147991 (Accession XM_085993). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147991. LOC149386 (Accession XM_097631) is another VGAM1019 host target gene. LOC149386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149386 BINDING SITE, designated SEQ ID:40986, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37587] Another function of VGAM1019 is therefore inhibition of LOC149386 (Accession XM_097631). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149386. LOC150378 (Accession XM_086857) is another VGAM1019 host target gene. LOC150378 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150378 BINDING SITE, designated SEQ ID:38923, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37588] Another function of VGAM1019 is therefore inhibition of LOC150378 (Accession XM_086857). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150378. LOC151194 (Accession NM_145280) is another VGAM1019 host target gene. LOC151194 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151194 BINDING SITE, designated SEQ ID:29797, to

the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37589] Another function of VGAM1019 is therefore inhibition of LOC151194 (Accession NM_145280). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151194. LOC152402 (Accession XM_098222) is another VGAM1019 host target gene. LOC152402 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152402 BINDING SITE, designated SEQ ID:41495, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37590] Another function of VGAM1019 is therefore inhibition of LOC152402 (Accession XM_098222). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152402. LOC152633 (Accession XM_098248) is another VGAM1019 host target gene. LOC152633 BINDING SITE is HOST TARGET binding site found in the 5` un-

translated region of mRNA encoded by LOC152633, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152633 BINDING SITE, designated SEQ ID:41533, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37591] Another function of VGAM1019 is therefore inhibition of LOC152633 (Accession XM_098248). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152633. LOC201116 (Accession XM_113896) is another VGAM1019 host target gene. LOC201116 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201116 BINDING SITE, designated SEQ ID:42525, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37592] Another function of VGAM1019 is therefore inhibition of LOC201116 (Accession XM_113896). Accordingly, utilities

of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201116. LOC253142 (Accession XM_173229) is another VGAM1019 host target gene. LOC253142 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253142 BINDING SITE, designated SEQ ID:46501, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37593] Another function of VGAM1019 is therefore inhibition of LOC253142 (Accession XM_173229). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253142. LOC254065 (Accession XM_173239) is another VGAM1019 host target gene. LOC254065 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC254065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC254065 BINDING SITE, designated SEQ ID:46520, to the nucleotide sequence of VGAM1019 RNA, herein designated VGAM RNA, also designated SEQ ID:3730.

[37594] Another function of VGAM1019 is therefore inhibition of LOC254065 (Accession XM_173239). Accordingly, utilities of VGAM1019 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254065. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1020 (VGAM1020) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37595] VGAM1020 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1020 was detected is described hereinabove with reference to Figs. 1–8.

[37596] VGAM1020 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37597] VGAM1020 gene encodes a VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1020 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1020 precursor RNA is designated SEQ ID:1006, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1006 is located at position 3793 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

[37598] VGAM1020 precursor RNA folds onto itself, forming VGAM1020 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37599] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1020 folded precursor RNA into VGAM1020 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1020 RNA is designated SEQ ID:3731, and is provided hereinbelow with reference to the sequence listing part.

[37600] VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1020 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37601] VGAM1020 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1020 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1020 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[37602] The complementary binding of VGAM1020 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1020 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1020 host target RNA into VGAM1020 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37603] It is appreciated that VGAM1020 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1020 host target genes. The mRNA of each one of this plurality of VGAM1020 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1020 RNA, herein designated VGAM RNA, and which when bound by VGAM1020 RNA causes inhibition of translation of respective one or more VGAM1020 host target proteins.

[37604] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1020 gene, herein designated VGAM GENE, on one or more VGAM1020 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[37605] It is yet further appreciated that a function of VGAM1020 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1020 correlate with, and may be deduced from, the identity of the host target genes which VGAM1020 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37606] Nucleotide sequences of the VGAM1020 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1020 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1020 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1020 are further described hereinbelow with reference to Table 1.

[37607] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1020 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1020 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37608] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1020 gene, herein designated VGAM is inhibition of expression of VGAM1020 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1020 correlate with, and may be deduced from, the identity of the target genes which VGAM1020 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37609] Acetylcholinesterase (YT blood group) (ACHE, Accession NM_015831) is a VGAM1020 host target gene. ACHE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACHE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACHE BINDING SITE, designated SEQ ID:17942, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37610] A function of VGAM1020 is therefore inhibition of Acetyl-

cholinesterase (YT blood group) (ACHE, Accession NM_015831), a gene which rapidly hydrolyzes choline released into the synapse. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACHE. The function of ACHE has been established by previous studies. Coates and Simpson (1972) concluded that 3 phenotypic variants of acetylcholinesterase (EC 3.1.1.7) result from 2 codominant alleles at a single locus. Rondino et al. (1988) showed that all the forms of acetylcholinesterase observed in avian nerves and muscle are encoded by a single autosomal gene. Differences in assembly and localization of the multiple synaptic forms of acetylcholinesterase are thought to arise through post-transcriptional events. Lapidot-Lifson et al. (1989) referred to the cloning of the gene for acetylcholinesterase. They used these clones to study the coamplification of acetylcholinesterase and pseudocholinesterase (butyrylcholinesterase; BCHE; 177400). Their coamplification in certain leukemias and in disorders of platelet formation suggest that the 2 loci may be linked. (The pseudocholinesterase gene is located at 3q25.2.) Whereas pseudocholinesterase is a soluble plasma enzyme pre-

sumed to be produced by the liver but also present in muscle and brain, acetylcholinesterase or 'true' cholinesterase is involved in the signal transmission at neuromuscular junctions and is also intensely expressed in the human central nervous system and the erythrocyte membrane. That such was the case was demonstrated by Getman et al. (1992). By chromosomal in situ suppression hybridization analysis, they showed that a single gene is located at 7q22 and confirmed the results by PCR analysis of genomic DNA from a human/hamster somatic cell hybrid containing a single human chromosome 7. Thus the gene maps to the same region that is frequently the site of nonrandom deletion in leukemias of myeloid cell precursors known to express acetylcholinesterase during normal differentiation. Animal model experiments lend further support to the function of ACHE. Feng et al. (1999) generated ColQ (OMIM Ref. No. 603033) –/– mice to study the roles played by ColQ and AChE in synapses and elsewhere.

[37611] It is appreciated that the abovementioned animal model for ACHE is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

- [37612] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [37613] Lapidot–Lifson, Y.; Prody, C. A.; Ginzberg, D.; Meytes, D.; Zakut, H.; Soreq, H. : Coamplification of human acetylcholinesterase and butyrylcholinesterase genes in blood cells: correlation with various leukemias and abnormal megakaryocytopoiesis. Proc. Nat. Acad. Sci. 86: 4715–4719, 1989. ; and
- [37614] Feng, G.; Krejci, E.; Molgo, J.; Cunningham, J. M.; Massoulie, J.; Sanes, J. R. : Genetic analysis of collagen Q: roles in acetylcholinesterase and butyrylcholinesterase assembly and in.
- [37615] Further studies establishing the function and utilities of ACHE are found in John Hopkins OMIM database record ID 100740, and in cited publications numbered 4120–412 and 4224 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adducin 1 (alpha) (ADD1, Accession NM_014190) is another VGAM1020 host target gene. ADD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ADD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD1 BINDING SITE, designated SEQ ID:15472, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37616] Another function of VGAM1020 is therefore inhibition of Adducin 1 (alpha) (ADD1, Accession NM_014190), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD1. The function of ADD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM474.UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_006057) is another VGAM1020 host target gene. B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT5

BINDING SITE1 through B3GALT5 BINDING SITE5, designated SEQ ID:12697, SEQ ID:27021, SEQ ID:27025, SEQ ID:27030 and SEQ ID:27035 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37617] Another function of VGAM1020 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_006057). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT5. Cysteine-rich Motor Neuron 1 (CRIM1, Accession NM_016441) is another VGAM1020 host target gene. CRIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRIM1 BINDING SITE, designated SEQ ID:18560, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37618] Another function of VGAM1020 is therefore inhibition of Cysteine-rich Motor Neuron 1 (CRIM1, Accession

NM_016441). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRIM1. Epithelial Membrane Protein 1 (EMP1, Accession NM_001423) is another VGAM1020 host target gene. EMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMP1 BINDING SITE, designated SEQ ID:7133, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37619] Another function of VGAM1020 is therefore inhibition of Epithelial Membrane Protein 1 (EMP1, Accession NM_001423), a gene which plays a role in squamous cell differentiation; member of the PMP22/EMP/MP20 family of membrane glycoproteins. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMP1. The function of EMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM107.Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM_003950) is another VGAM1020 host target gene. F2RL3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by F2RL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2RL3 BINDING SITE, designated SEQ ID:10081, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37620] Another function of VGAM1020 is therefore inhibition of Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM_003950), a gene which Protease-activated receptor 4; G protein-coupled receptor that increases phosphoinositide hydrolysis. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F2RL3. The function of F2RL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193.Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_004961) is another

VGAM1020 host target gene. GABRE BINDING SITE1 through GABRE BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GABRE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABRE BINDING SITE1 through GABRE BINDING SITE4, designated SEQ ID:11408, SEQ ID:22510, SEQ ID:22514 and SEQ ID:22531 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37621] Another function of VGAM1020 is therefore inhibition of Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_004961), a gene which mediates neuronal inhibition by binding to the gaba/benzodiazepine receptor and opening an integral chloride channel. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABRE. The function of GABRE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259.Glutamate-ammonia Ligase (glutamine syn-

thase) (GLUL, Accession NM_002065) is another VGAM1020 host target gene. GLUL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUL BINDING SITE, designated SEQ ID:7835, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37622] Another function of VGAM1020 is therefore inhibition of Glutamate-ammonia Ligase (glutamine synthase) (GLUL, Accession NM_002065), a gene which catalyzes the condensation of glutamate and ammonia to form glutamine. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUL. The function of GLUL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM948. Hairless Homolog (mouse) (HR, Accession NM_005144) is another VGAM1020 host target gene. HR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by HR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HR BINDING SITE, designated SEQ ID:11617, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37623] Another function of VGAM1020 is therefore inhibition of Hairless Homolog (mouse) (HR, Accession NM_005144). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HR. Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3, Accession NM_005501) is another VGAM1020 host target gene. ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ITGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2, designated SEQ ID:12009 and SEQ ID:7966 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3731.

[37624] Another function of VGAM1020 is therefore inhibition of Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3, Accession NM_005501), a gene which is a receptor for fibronectin, laminin, collagen, epiligrin and thrombospondin. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA3. The function of ITGA3 has been established by previous studies. Integrins are a family of cell surface adhesion molecules. Each integrin consists of a pair of noncovalently associated alpha and beta chains. Integrin alpha-chain sequences are characterized by a 7-fold repeated amino acid motif, of which the last 3 or 4 contain divalent cation-binding sites. The ITGA3 subunit is associated with ITGB1 (OMIM Ref. No. 135630). By screening a bladder carcinoma cDNA library with a hamster galactoprotein B3 (Gapb3) probe, Tsuji et al. (1991) isolated cDNAs encoding ITGA3. The deduced 1,019-amino acid mature ITGA3 protein contains 14 potential N-glycosylation sites and a potential cleavage site. Northern blot analysis detected a 4.8-kb ITGA3 transcript whose expression was induced by SV-40 transformation. By immunoscreening an endothe-

lial cell cDNA library for ITGA3 protein, Takada et al. (1991) obtained an ITGA3 cDNA. Western blot analysis showed that recombinant ITGA3 was expressed as a 150-kD protein, the same size as the native protein. The deduced 1,051-amino acid ITGA3 protein has a 32-amino acid signal peptide, a 28-amino acid transmembrane domain, and a 32-amino acid cytoplasmic segment. ITGA3 also contains 13 potential N-glycosylation sites, 2 potential cleavage sites, and the 7 N-terminal repeating units characteristic of ITGAs. Northern blot analysis detected a 5-kb ITGA3 transcript in fibroblasts. Jones et al. (1998) determined that the ITGA3 gene spans 36.3 kb and contains 26 exons. By searching for sequences related to murine Itga3, Jones et al. (1998) identified a chromosome 17 clone corresponding to ITGA3. Human herpesvirus-8 (HHV-8) is implicated in the pathogenesis of Kaposi sarcoma. HHV-8 envelope glycoprotein B possesses the RGD amino acid motif known to interact with integrin molecules. Akula et al. (2002) found that HHV-8 infectivity was inhibited by RGD peptides, antibodies against the RGD-dependent integrins ITGA3 and ITGB1, and by soluble ITGA3/ITGB1. Expression of human ITGA3 increased the infectivity of virus for Chinese hamster ovary cells.

Anti-glycoprotein B antibodies immunoprecipitated the virus-ITGA3 and -ITGB1 complexes, and virus-binding studies suggested a role for ITGA3/ITGB1 in HHV-8 entry. Further, HHV-8 infection induced the integrin-mediated activation of focal adhesion kinase (FAK; 600758). These findings implicated a role for ITGA3/ITGB1 and the associated signaling pathways in HHV-8 entry into target cells.

[37625] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37626] Akula, S. M.; Pramod, N. P.; Wang, F.-Z.; Chandran, B. : Integrin alpha-3/beta-1 (CD 49c/29) is a cellular receptor for Kaposi's sarcoma-associated herpesvirus (KSHV/HHV-8) entry into the target cells. Cell 108: 407-419, 2002. ; and

[37627] Jones, S. D.; van der Flier, A.; Sonnenberg, A. : Genomic organization of the human alpha-3 integrin subunit gene. Biochem. Biophys. Res. Commun. 248: 896-898, 1998.

[37628] Further studies establishing the function and utilities of ITGA3 are found in John Hopkins OMIM database record ID 605025, and in cited publications numbered 334 and 4796-4798 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Microtubule-associated Protein 1B (MAP1B, Accession NM_005909) is another VGAM1020 host target gene. MAP1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1B BINDING SITE, designated SEQ ID:12534, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37629] Another function of VGAM1020 is therefore inhibition of Microtubule-associated Protein 1B (MAP1B, Accession NM_005909), a gene which may have a role in neuronal plasticity and brain development. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1B. The function of MAP1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM316. RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession NM_002877) is another VGAM1020 host target gene. RAD51L1 BINDING SITE1 and RAD51L1 BINDING

SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD51L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD51L1 BINDING SITE1 and RAD51L1 BINDING SITE2, designated SEQ ID:8786 and SEQ ID:28575 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37630] Another function of VGAM1020 is therefore inhibition of RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession NM_002877), a gene which is a member of the RAD51 family of strand-transfer proteins. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD51L1. The function of RAD51L1 has been established by previous studies. The *E. coli* RecA protein plays a major role in recombination and repair. The *S. cerevisiae* RAD51 protein is homologous to RecA and functions in both mitotic and meiotic homologous recombination and in double-stranded break repair. See RAD51A (OMIM Ref. No. 179617). By computerized searching of an EST database, Albala et al. (1997) identified human and mouse cDNAs

encoding a protein with homology to RAD51. The predicted 350-amino acid human protein, designated RAD51B by them, shares 27 to 30% sequence identity with yeast and chicken RAD51 and human RAD51A. RAD51B contains conserved nucleotide-binding motifs, suggesting that it is an ATPase. Northern blot analysis revealed that RAD51B was expressed as a 1.8-kb mRNA in all tissues examined. In both mouse and human, the highest levels of expression were seen in testis, thymus, ovary, and spleen, tissues that undergo recombination events.

[37631] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37632] Albala, J. S.; Thelen, M. P.; Prange, C.; Fan, W.; Christensen, M.; Thompson, L. H.; Lennon, G. G. : Identification of a novel human RAD51 homolog, RAD51B. *Genomics* 46: 476-479, 1997. ; and

[37633] Masson, J.-Y.; Tarsounas, M. C.; Stasiak, A. Z.; Stasiak, A.; Shah, R.; McIlwraith, M. J.; Benson, F. E.; West, S. C. : Identification and purification of two distinct complexes containing.

[37634] Further studies establishing the function and utilities of RAD51L1 are found in John Hopkins OMIM database

record ID 602948, and in cited publications numbered 1056–1057, 2743–1603, 105 and 1692 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM1020 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28445, SEQ ID:28462 and SEQ ID:11347 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37635] Another function of VGAM1020 is therefore inhibition of Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various

diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152) is another VGAM1020 host target gene. C20orf12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf12 BINDING SITE, designated SEQ ID:19956, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37636] Another function of VGAM1020 is therefore inhibition of Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf12. CREB-H (Accession NM_032607) is another VGAM1020 host target gene. CREB-H BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CREB-H, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CREB-H BINDING SITE, designated SEQ ID:26330, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37637] Another function of VGAM1020 is therefore inhibition of CREB-H (Accession NM_032607). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREB-H. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12 (CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM_006936) is another VGAM1020 host target gene. DDX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX12 BINDING SITE, designated SEQ ID:30023, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37638] Another function of VGAM1020 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 12

(CHL1-like helicase homolog, *S. cerevisiae*) (DDX12, Accession XM_006936). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX12. DKFZp566H0824 (Accession NM_017535) is another VGAM1020 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated SEQ ID:18973, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37639] Another function of VGAM1020 is therefore inhibition of DKFZp566H0824 (Accession NM_017535). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. FLJ11259 (Accession NM_018370) is another VGAM1020 host target gene. FLJ11259 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11259, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11259 BINDING SITE, designated SEQ ID:20384, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37640] Another function of VGAM1020 is therefore inhibition of FLJ11259 (Accession NM_018370). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11259. FLJ14327 (Accession NM_024912) is another VGAM1020 host target gene. FLJ14327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14327 BINDING SITE, designated SEQ ID:24428, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37641] Another function of VGAM1020 is therefore inhibition of FLJ14327 (Accession NM_024912). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14327. Forkhead Box D4 (FOXD4, Accession XM_095746) is another VGAM1020 host target gene. FOXD4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FOXD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXD4 BINDING SITE, designated SEQ ID:40282, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37642] Another function of VGAM1020 is therefore inhibition of Forkhead Box D4 (FOXD4, Accession XM_095746). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXD4. Integrin, Alpha 10 (ITGA10, Accession XM_002097) is another VGAM1020 host target gene. ITGA10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITGA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ITGA10 BINDING SITE, designated SEQ ID:29865, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37643] Another function of VGAM1020 is therefore inhibition of Integrin, Alpha 10 (ITGA10, Accession XM_002097). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA10. KIAA0544 (Accession XM_048119) is another VGAM1020 host target gene. KIAA0544 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0544, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0544 BINDING SITE, designated SEQ ID:35113, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37644] Another function of VGAM1020 is therefore inhibition of KIAA0544 (Accession XM_048119). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0544. KIAA0668 (Accession XM_039332) is another VGAM1020 host target gene. KIAA0668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0668 BINDING SITE, designated SEQ ID:33052, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37645] Another function of VGAM1020 is therefore inhibition of KIAA0668 (Accession XM_039332). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0668. KIAA0774 (Accession XM_166270) is another VGAM1020 host target gene. KIAA0774 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0774, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0774 BINDING SITE, designated SEQ ID:44091, to the nucleotide sequence of VGAM1020 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3731.

[37646] Another function of VGAM1020 is therefore inhibition of KIAA0774 (Accession XM_166270). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0774. KIAA0789 (Accession XM_033113) is another VGAM1020 host target gene. KIAA0789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0789 BINDING SITE, designated SEQ ID:31848, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37647] Another function of VGAM1020 is therefore inhibition of KIAA0789 (Accession XM_033113). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0789. KIAA1855 (Accession XM_166453) is another VGAM1020 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44352, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37648] Another function of VGAM1020 is therefore inhibition of KIAA1855 (Accession XM_166453). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. MGC12538 (Accession NM_032746) is another VGAM1020 host target gene. MGC12538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12538 BINDING SITE, designated SEQ ID:26482, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37649] Another function of VGAM1020 is therefore inhibition of MGC12538 (Accession NM_032746). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC12538. MIC2 Like 1 (MIC2L1, Accession NM_031462) is another VGAM1020 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25491, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37650] Another function of VGAM1020 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM_031462). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. NFASC (Accession XM_046808) is another VGAM1020 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34832, to the nucleotide se-

quence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37651] Another function of VGAM1020 is therefore inhibition of NFASC (Accession XM_046808). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. PEPP3 (Accession NM_014935) is another VGAM1020 host target gene. PEPP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEPP3 BINDING SITE, designated SEQ ID:17234, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37652] Another function of VGAM1020 is therefore inhibition of PEPP3 (Accession NM_014935). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEPP3. Sialyltransferase 4A (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM_003033) is another VGAM1020 host target gene. SIAT4A BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT4A BINDING SITE, designated SEQ ID:8981, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37653] Another function of VGAM1020 is therefore inhibition of Sialyltransferase 4A (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4A, Accession NM_003033). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT4A. Signal-regulatory Protein Beta 1 (SIRPB1, Accession NM_006065) is another VGAM1020 host target gene. SIRPB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIRPB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIRPB1 BINDING SITE, designated SEQ ID:12708, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3731.

[37654] Another function of VGAM1020 is therefore inhibition of Signal-regulatory Protein Beta 1 (SIRPB1, Accession NM_006065). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIRPB1. STRAIT11499 (Accession NM_021242) is another VGAM1020 host target gene. STRAIT11499 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRAIT11499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRAIT11499 BINDING SITE, designated SEQ ID:22212, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37655] Another function of VGAM1020 is therefore inhibition of STRAIT11499 (Accession NM_021242). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRAIT11499. Zinc Finger Protein 339 (ZNF339, Accession NM_021220) is another VGAM1020 host target gene. ZNF339 BINDING SITE is HOST TARGET binding site

found in the 5' untranslated region of mRNA encoded by ZNF339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF339 BINDING SITE, designated SEQ ID:22199, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37656] Another function of VGAM1020 is therefore inhibition of Zinc Finger Protein 339 (ZNF339, Accession NM_021220). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF339. LOC129676 (Accession XM_065341) is another VGAM1020 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37286, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37657] Another function of VGAM1020 is therefore inhibition of LOC129676 (Accession XM_065341). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129676. LOC132299 (Accession XM_059584) is another VGAM1020 host target gene. LOC132299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC132299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132299 BINDING SITE, designated SEQ ID:37023, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37658] Another function of VGAM1020 is therefore inhibition of LOC132299 (Accession XM_059584). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132299. LOC143287 (Accession XM_096410) is another VGAM1020 host target gene. LOC143287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143287, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143287 BINDING SITE, designated SEQ ID:40345, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37659] Another function of VGAM1020 is therefore inhibition of LOC143287 (Accession XM_096410). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143287. LOC144110 (Accession XM_084735) is another VGAM1020 host target gene. LOC144110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144110 BINDING SITE, designated SEQ ID:37681, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37660] Another function of VGAM1020 is therefore inhibition of LOC144110 (Accession XM_084735). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC144110. LOC144373 (Accession XM_084841) is another VGAM1020 host target gene. LOC144373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144373 BINDING SITE, designated SEQ ID:37728, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37661] Another function of VGAM1020 is therefore inhibition of LOC144373 (Accession XM_084841). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144373. LOC145622 (Accession XM_085186) is another VGAM1020 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37911, to the nucleotide sequence of VGAM1020 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3731.

[37662] Another function of VGAM1020 is therefore inhibition of LOC145622 (Accession XM_085186). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC146520 (Accession XM_085492) is another VGAM1020 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38187, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37663] Another function of VGAM1020 is therefore inhibition of LOC146520 (Accession XM_085492). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC146953 (Accession XM_085659) is another VGAM1020 host target gene. LOC146953 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146953, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146953 BINDING SITE, designated SEQ ID:38286, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37664] Another function of VGAM1020 is therefore inhibition of LOC146953 (Accession XM_085659). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146953. LOC152283 (Accession XM_098196) is another VGAM1020 host target gene. LOC152283 BINDING SITE1 and LOC152283 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC152283, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152283 BINDING SITE1 and LOC152283 BINDING SITE2, designated SEQ ID:41486 and SEQ ID:41487 respectively, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37665] Another function of VGAM1020 is therefore inhibition of

LOC152283 (Accession XM_098196). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152283. LOC155389 (Accession XM_088229) is another VGAM1020 host target gene. LOC155389 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155389 BINDING SITE, designated SEQ ID:39562, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37666] Another function of VGAM1020 is therefore inhibition of LOC155389 (Accession XM_088229). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155389. LOC221218 (Accession XM_166281) is another VGAM1020 host target gene. LOC221218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC221218 BINDING SITE, designated SEQ ID:44092, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37667] Another function of VGAM1020 is therefore inhibition of LOC221218 (Accession XM_166281). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221218. LOC253451 (Accession XM_171151) is another VGAM1020 host target gene. LOC253451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253451 BINDING SITE, designated SEQ ID:45948, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37668] Another function of VGAM1020 is therefore inhibition of LOC253451 (Accession XM_171151). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253451. LOC256974 (Accession XM_173190) is an-

other VGAM1020 host target gene. LOC256974 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256974, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256974 BINDING SITE, designated SEQ ID:46436, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37669] Another function of VGAM1020 is therefore inhibition of LOC256974 (Accession XM_173190). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256974. LOC90495 (Accession XM_032166) is another VGAM1020 host target gene. LOC90495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90495 BINDING SITE, designated SEQ ID:31579, to the nucleotide sequence of VGAM1020 RNA, herein designated VGAM RNA, also designated SEQ ID:3731.

[37670] Another function of VGAM1020 is therefore inhibition of LOC90495 (Accession XM_032166). Accordingly, utilities of VGAM1020 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90495. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1021 (VGAM1021) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37671] VGAM1021 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1021 was detected is described hereinabove with reference to Figs. 1–8.

[37672] VGAM1021 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37673] VGAM1021 gene encodes a VGAM1021 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1021 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1021 precursor RNA is designated SEQ ID:1007, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1007 is located at position 2132 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

- [37674] VGAM1021 precursor RNA folds onto itself, forming VGAM1021 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [37675] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1021 folded precursor RNA into VGAM1021 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1021 RNA is designated SEQ ID:3732, and is provided hereinbelow with reference to the sequence listing part.

[37676] VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1021 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[37677] VGAM1021 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1021 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1021 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37678] The complementary binding of VGAM1021 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1021 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1021 host target RNA into VGAM1021 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37679] It is appreciated that VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1021 host target genes. The mRNA of each one of this plurality of VGAM1021 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1021 RNA, herein designated VGAM RNA, and which when bound by VGAM1021 RNA causes inhibition of translation of respective one or more VGAM1021 host target proteins.

[37680] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1021 gene, herein designated VGAM GENE, on one or more VGAM1021 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37681] It is yet further appreciated that a function of VGAM1021 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1021 correlate with, and may be deduced from, the identity of the host target genes which VGAM1021 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37682] Nucleotide sequences of the VGAM1021 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1021 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1021 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1021 are further described hereinbelow with reference to Table 1.

[37683] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM1021 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1021 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[37684] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1021 gene, herein designated VGAM is inhibition of expression of VGAM1021 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1021 correlate with, and may be deduced from, the identity of the target genes which VGAM1021 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37685] Centrosomal Protein 2 (CEP2, Accession NM_006779) is a VGAM1021 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:13652, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37686] A function of VGAM1021 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM_006779), a gene which interacts with TC10 and CDC42. Accordingly, utilities of VGAM1021 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. Dystrobrevin, Alpha (DTNA, Accession NM_001391) is another VGAM1021 host target gene. DTNA BINDING SITE1 through DTNA BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DTNA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTNA BINDING SITE1 through DTNA BINDING SITE4, designated SEQ ID:7080, SEQ ID:26838, SEQ ID:26843 and SEQ ID:26848 respectively, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37687] Another function of VGAM1021 is therefore inhibition of Dystrobrevin, Alpha (DTNA, Accession NM_001391), a gene which may be involved in the formation and stability of synapses. Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DTNA. The function of

DTNA has been established by previous studies. The dystrophin-associated protein complex (DPC), located at the sarcolemma, can be divided into 3 subcomplexes: the dystroglycan complex, the sarcoglycan complex, and the cytoplasmic complex. The last consists of 2 families of proteins, the syntrophins and dystrobrevin. Metzinger et al. (1997) found that anti-dystrobrevin antibodies stain the sarcolemma in normal skeletal muscle, indicating that dystrobrevin colocalizes with dystrophin and the dystrophin-associated protein complex. By contrast, dystrobrevin membrane staining was severely reduced in muscles of Duchenne muscular dystrophy patients and also dramatically reduced in patients with limb-girdle muscular dystrophy arising from the loss of 1 or all of the sarcoglycan components (e.g., LGMD2C; 253700). Normal dystrobrevin staining was observed in patients with other forms of limb-girdle muscular dystrophy where dystrophin and the rest of the dystrophin-associated protein complex are normally expressed (e.g., LGMD2A; 253600), as well as in other neuromuscular disorders. Their results showed that dystrobrevin deficiency is a generic feature of dystrophies linked to dystrophin and the dystrophin-associated proteins. This was the first indication that a cyto-

plasmic component of the dystrophin-associated protein complex may be involved in the pathogenesis of limb-girdle muscular dystrophy. Left ventricular noncompaction (LVNC) is due to an arrest of myocardial morphogenesis. The disorder is characterized by a hypertrophic left ventricular with deep trabeculations and with poor systolic function, with or without associated left ventricular dilation. In some cases, the right ventricle is also affected. LVNC may be isolated (see OMIM Ref. No. 300183 and 604169) or associated with congenital heart anomalies such as ventricular septal defects, pulmonic stenosis, and atrial septal defects. Ichida et al. (2001) screened the DTNA gene in a Japanese family in which members of 4 generations were affected, 5 with LVNC associated with congenital heart defects (OMIM Ref. No. 606617) and 1 with isolated LVNC. They found a missense mutation in the DTNA gene, P121L (601239.0001).

[37688] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37689] Ichida, F.; Tsubata, S.; Bowles, K. R.; Haneda, N.; Uese, K.; Miyawaki, T.; Dreyer, W. J.; Messina, J.; Li, H.; Bowles, N. E.; Towbin, J. A. : Novel gene mutations in patients with

left ventricular noncompaction or Barth syndrome. Circulation 103: 1256–1263, 2001. ; and

[37690] Metzinger, L.; Blake, D. J.; Squier, M. V.; Anderson, L. V. B.; Deconinck, A. E.; Nawrotzki, R.; Hilton–Jones, D.; Davies, K. E. : Dystrobrevin deficiency at the sarcolemma of patients.

[37691] Further studies establishing the function and utilities of DTNA are found in John Hopkins OMIM database record ID 601239, and in cited publications numbered 2841–2843, 751 and 7517–7520 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM_133367) is another VGAM1021 host target gene. C6orf33 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C6orf33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf33 BINDING SITE, designated SEQ ID:28493, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37692] Another function of VGAM1021 is therefore inhibition of

Chromosome 6 Open Reading Frame 33 (C6orf33, Accession NM_133367). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf33. KIAA0089 (Accession XM_046056) is another VGAM1021 host target gene. KIAA0089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0089 BINDING SITE, designated SEQ ID:34667, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37693] Another function of VGAM1021 is therefore inhibition of KIAA0089 (Accession XM_046056). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0089. Phosphatidylserine Decarboxylase (PISD, Accession NM_014338) is another VGAM1021 host target gene. PISD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PISD, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PISD BINDING SITE, designated SEQ ID:15657, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37694] Another function of VGAM1021 is therefore inhibition of Phosphatidylserine Decarboxylase (PISD, Accession NM_014338). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PISD. PNAS-127 (Accession NM_032490) is another VGAM1021 host target gene. PNAS-127 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PNAS-127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNAS-127 BINDING SITE, designated SEQ ID:26241, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37695] Another function of VGAM1021 is therefore inhibition of PNAS-127 (Accession NM_032490). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with PNAS-127. Williams Beuren Syndrome Chromosome Region 21 (WBSCR21, Accession NM_031295) is another VGAM1021 host target gene. WBSCR21 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by WBSCR21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR21 BINDING SITE, designated SEQ ID:25326, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37696] Another function of VGAM1021 is therefore inhibition of Williams Beuren Syndrome Chromosome Region 21 (WBSCR21, Accession NM_031295). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR21. LOC149721 (Accession XM_086649) is another VGAM1021 host target gene. LOC149721 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC149721 BINDING SITE, designated SEQ ID:38809, to the nucleotide sequence of VGAM1021 RNA, herein designated VGAM RNA, also designated SEQ ID:3732.

[37697] Another function of VGAM1021 is therefore inhibition of LOC149721 (Accession XM_086649). Accordingly, utilities of VGAM1021 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149721. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1022 (VGAM1022) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37698] VGAM1022 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1022 was detected is described hereinabove with reference to Figs. 1–8.

[37699] VGAM1022 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[37700] VGAM1022 gene encodes a VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1022 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1022 precursor RNA is designated SEQ ID:1008, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1008 is located at position 2327 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

[37701] VGAM1022 precursor RNA folds onto itself, forming VGAM1022 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37702] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1022 folded precursor RNA into VGAM1022 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1022 RNA is designated SEQ ID:3733, and is provided hereinbelow with reference to the sequence listing part.

[37703] VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1022 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37704] VGAM1022 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1022 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1022 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37705] The complementary binding of VGAM1022 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1022 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1022 host target RNA into VGAM1022 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37706] It is appreciated that VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1022 host target genes. The mRNA of each one of this plurality of VGAM1022 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1022 RNA, herein designated VGAM RNA, and which when bound by VGAM1022 RNA causes inhibition of translation of respective one or more VGAM1022 host target proteins.

[37707] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1022 gene, herein designated VGAM GENE, on one or more VGAM1022 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37708] It is yet further appreciated that a function of VGAM1022 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1022 correlate with, and may be deduced from, the identity of the host target genes which VGAM1022 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37709] Nucleotide sequences of the VGAM1022 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1022 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1022 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1022 are further described hereinbelow with reference to Table 1.

[37710] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of

Fig. 1, found on VGAM1022 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1022 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37711] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1022 gene, herein designated VGAM is inhibition of expression of VGAM1022 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1022 correlate with, and may be deduced from, the identity of the target genes which VGAM1022 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37712] Calsequestrin 2 (cardiac muscle) (CASQ2, Accession NM_001232) is a VGAM1022 host target gene. CASQ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASQ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASQ2 BINDING SITE, designated SEQ ID:6902, to the nucleotide sequence of VGAM1022 RNA, herein designated VGAM RNA, also designated SEQ ID:3733.

[37713] A function of VGAM1022 is therefore inhibition of Calsequestrin 2 (cardiac muscle) (CASQ2, Accession NM_001232). Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASQ2. RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884) is another VGAM1022 host target gene. RAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP1A BINDING SITE, designated SEQ ID:8792, to the nucleotide sequence of VGAM1022 RNA, herein designated VGAM RNA, also designated SEQ ID:3733.

[37714] Another function of VGAM1022 is therefore inhibition of RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884), a gene which induces morphological reversion of a cell line transformed by a ras oncogene. Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP1A. The function of RAP1A and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM993.DKFZp547I094 (Accession NM_032155) is another VGAM1022 host target gene. DKFZp547I094 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547I094, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I094 BINDING SITE, designated SEQ ID:25855, to the nucleotide sequence of VGAM1022 RNA, herein designated VGAM RNA, also designated SEQ ID:3733.

[37715] Another function of VGAM1022 is therefore inhibition of DKFZp547I094 (Accession NM_032155). Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I094. MGC11082 (Accession NM_032691) is another VGAM1022 host target gene. MGC11082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC11082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of MGC11082 BINDING SITE, designated SEQ ID:26411, to the nucleotide sequence of VGAM1022 RNA, herein designated VGAM RNA, also designated SEQ ID:3733.

[37716] Another function of VGAM1022 is therefore inhibition of MGC11082 (Accession NM_032691). Accordingly, utilities of VGAM1022 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11082. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1023 (VGAM1023) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37717] VGAM1023 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1023 was detected is described hereinabove with reference to Figs. 1–8.

[37718] VGAM1023 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[37719] VGAM1023 gene encodes a VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1023 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1023 precursor RNA is designated SEQ ID:1009, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1009 is located at position 3936 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

[37720] VGAM1023 precursor RNA folds onto itself, forming VGAM1023 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37721] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1023 folded precursor RNA into VGAM1023 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1023 RNA is designated SEQ ID:3734, and is provided hereinbelow with reference to the sequence listing part.

[37722] VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1023 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37723] VGAM1023 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1023 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1023 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37724] The complementary binding of VGAM1023 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1023 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1023 host target RNA into VGAM1023 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37725] It is appreciated that VGAM1023 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1023 host target genes. The mRNA of each one of this plurality of VGAM1023 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1023 RNA, herein designated VGAM RNA, and which when bound by VGAM1023 RNA causes inhibition of translation of respective one or more VGAM1023 host target proteins.

[37726] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1023 gene, herein designated VGAM GENE, on one or more VGAM1023 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[37727] It is yet further appreciated that a function of VGAM1023 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1023 correlate with, and may be deduced from, the identity of the host target genes which VGAM1023 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37728] Nucleotide sequences of the VGAM1023 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1023 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1023 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1023 are further described hereinbelow with reference to Table 1.

[37729] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM1023 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1023 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37730] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1023 gene, herein designated VGAM is inhibition of expression of VGAM1023 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1023 correlate with, and may be deduced from, the identity of the target genes which VGAM1023 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37731] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession NM_144767) is a VGAM1023 host target gene. AKAP13 BINDING SITE1 through AKAP13 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AKAP13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE1 through AKAP13 BINDING SITE3, designated SEQ ID:29558, SEQ ID:13589 and SEQ ID:14054 respectively, to the nucleotide sequence of VGAM1023 RNA, herein

designated VGAM RNA, also designated SEQ ID:3734.

[37732] A function of VGAM1023 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession NM_144767), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17. Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession NM_031364) is another VGAM1023 host target gene. COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3, designated SEQ ID:25357, SEQ ID:5544 and SEQ ID:19255 respectively, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37733] Another function of VGAM1023 is therefore inhibition of Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession NM_031364). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A3. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962) is another VGAM1023 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30970, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37734] Another function of VGAM1023 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA0522 (Accession XM_050404) is another VGAM1023 host target gene. KIAA0522 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by KIAA0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0522 BINDING SITE, designated SEQ ID:35621, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37735] Another function of VGAM1023 is therefore inhibition of KIAA0522 (Accession XM_050404). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0522. LOC145717 (Accession XM_039771) is another VGAM1023 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33187, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37736] Another function of VGAM1023 is therefore inhibition of

LOC145717 (Accession XM_039771). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC152925 (Accession XM_087559) is another VGAM1023 host target gene. LOC152925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152925 BINDING SITE, designated SEQ ID:39333, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37737] Another function of VGAM1023 is therefore inhibition of LOC152925 (Accession XM_087559). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152925. LOC158301 (Accession XM_088543) is another VGAM1023 host target gene. LOC158301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158301 BINDING SITE, designated SEQ ID:39808, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37738] Another function of VGAM1023 is therefore inhibition of LOC158301 (Accession XM_088543). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158301. LOC196957 (Accession XM_113789) is another VGAM1023 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42425, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37739] Another function of VGAM1023 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196957. LOC196961 (Accession XM_113790) is an-

other VGAM1023 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42434, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37740] Another function of VGAM1023 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM1023 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42452, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37741] Another function of VGAM1023 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC200014 (Accession XM_114087) is another VGAM1023 host target gene. LOC200014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42687, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37742] Another function of VGAM1023 is therefore inhibition of LOC200014 (Accession XM_114087). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. LOC202018 (Accession XM_114420) is another VGAM1023 host target gene. LOC202018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202018, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202018 BINDING SITE, designated SEQ ID:42956, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37743] Another function of VGAM1023 is therefore inhibition of LOC202018 (Accession XM_114420). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202018. LOC245727 (Accession XM_165913) is another VGAM1023 host target gene. LOC245727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC245727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245727 BINDING SITE, designated SEQ ID:43794, to the nucleotide sequence of VGAM1023 RNA, herein designated VGAM RNA, also designated SEQ ID:3734.

[37744] Another function of VGAM1023 is therefore inhibition of LOC245727 (Accession XM_165913). Accordingly, utilities of VGAM1023 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC245727. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1024 (VGAM1024) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37745] VGAM1024 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1024 was detected is described hereinabove with reference to Figs. 1–8.

[37746] VGAM1024 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37747] VGAM1024 gene encodes a VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1024 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1024 precursor RNA is designated SEQ ID:1010, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1010 is located at position 672 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

- [37748] VGAM1024 precursor RNA folds onto itself, forming VGAM1024 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed–reversed sequence of the nucleotide sequence of the second half thereof.
- [37749] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1024 folded precursor RNA into VGAM1024 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1024 RNA is designated SEQ ID:3735, and is provided hereinbelow with reference to the sequence listing part.

[37750] VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1024 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37751] VGAM1024 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1024 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1024 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37752] The complementary binding of VGAM1024 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1024 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1024 host target RNA into VGAM1024 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37753] It is appreciated that VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1024 host target genes. The mRNA of each one of this plurality of VGAM1024 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1024 RNA, herein designated VGAM RNA, and which when bound by VGAM1024 RNA causes

inhibition of translation of respective one or more VGAM1024 host target proteins.

[37754] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1024 gene, herein designated VGAM GENE, on one or more VGAM1024 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37755] It is yet further appreciated that a function of VGAM1024 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1024 include diagnosis, prevention and

treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1024 correlate with, and may be deduced from, the identity of the host target genes which VGAM1024 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37756] Nucleotide sequences of the VGAM1024 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1024 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1024 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1024 are further described hereinbelow with reference to Table 1.

[37757] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM1024 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1024 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37758] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1024 gene, herein designated VGAM is inhibition of expression of VGAM1024 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1024 correlate with, and may be deduced from, the identity of the target genes which VGAM1024 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37759] Retinoic Acid Induced 3 (RAI3, Accession NM_003979) is a VGAM1024 host target gene. RAI3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI3 BINDING SITE, designated SEQ ID:10111, to the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, also designated SEQ ID:3735.

[37760] A function of VGAM1024 is therefore inhibition of Retinoic Acid Induced 3 (RAI3, Accession NM_003979). Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI3. START Domain Containing 4, Sterol Regulated (STARD4, Accession NM_139164) is another VGAM1024 host target gene. STARD4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by STARD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STARD4 BINDING SITE, designated SEQ ID:29172, to the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, also designated SEQ ID:3735.

[37761] Another function of VGAM1024 is therefore inhibition of START Domain Containing 4, Sterol Regulated (STARD4, Accession NM_139164). Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD4. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662) is another VGAM1024 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19194, to the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, also designated SEQ ID:3735.

[37762] Another function of VGAM1024 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776) is another VGAM1024 host target gene. GIT2 BINDING SITE1 through GIT2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GIT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE1 through GIT2 BINDING SITE3, designated SEQ ID:16598, SEQ ID:27680 and SEQ ID:27693 respectively, to the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, also designated SEQ ID:3735.

[37763] Another function of VGAM1024 is therefore inhibition of G

Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776). Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. LOC90408 (Accession XM_031517) is another VGAM1024 host target gene. LOC90408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90408 BINDING SITE, designated SEQ ID:31396, to the nucleotide sequence of VGAM1024 RNA, herein designated VGAM RNA, also designated SEQ ID:3735.

[37764] Another function of VGAM1024 is therefore inhibition of LOC90408 (Accession XM_031517). Accordingly, utilities of VGAM1024 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90408. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1025 (VGAM1025) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[37765] VGAM1025 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1025 was detected is described hereinabove with reference to Figs. 1–8.

[37766] VGAM1025 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37767] VGAM1025 gene encodes a VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1025 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1025 precursor RNA is designated SEQ ID:1011, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1011 is located at position 3393 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

[37768] VGAM1025 precursor RNA folds onto itself, forming VGAM1025 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37769] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1025 folded precursor RNA into VGAM1025 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM1025 RNA is designated SEQ ID:3736, and is provided hereinbelow with reference to the sequence listing part.

[37770] VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1025 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37771] VGAM1025 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1025 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1025 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37772] The complementary binding of VGAM1025 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1025 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1025 host target RNA into VGAM1025 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37773] It is appreciated that VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1025 host target genes. The mRNA of each one of this plurality of VGAM1025 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1025 RNA, herein designated VGAM RNA, and which when bound by VGAM1025 RNA causes inhibition of translation of respective one or more VGAM1025 host target proteins.

[37774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1025 gene, herein designated VGAM GENE, on one or more VGAM1025 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37775] It is yet further appreciated that a function of VGAM1025 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1025 correlate with, and may be deduced from, the identity of the host target genes which VGAM1025 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[37776] Nucleotide sequences of the VGAM1025 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1025 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1025 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1025 are further described hereinbelow with reference to Table 1.

[37777] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1025 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1025 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37778] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1025 gene, herein designated VGAM is inhibition of expression of VGAM1025 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1025 correlate with, and may be deduced from, the identity of the target genes which VGAM1025 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37779] Annexin A7 (ANXA7, Accession NM_004034) is a VGAM1025 host target gene. ANXA7 BINDING SITE1 and ANXA7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANXA7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANXA7 BINDING SITE1 and ANXA7 BINDING SITE2, designated SEQ ID:10254 and SEQ ID:6825 respectively, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37780] A function of VGAM1025 is therefore inhibition of Annexin A7 (ANXA7, Accession NM_004034), a gene which promotes membrane fusion and is involved in exocytosis. Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANXA7. The function of ANXA7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM846. Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218) is

another VGAM1025 host target gene. KCNQ1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNQ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNQ1 BINDING SITE, designated SEQ ID:5725, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37781] Another function of VGAM1025 is therefore inhibition of Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218), a gene which probably important in cardiac repolarization. associates with kcne1 (mink) to form the i(ks) cardiac potassium current. elicits a rapidly activating, k(+)-selective outward current. muscarinic agonist oxotremorine-m strongly suppresses kcnq1/kcne1 current in cho cells in which cloned kcnq1/kcne1 channels were coexpressed with m1 muscarinic receptors. may associate also with kcne3 (mirp2) to form the potassium channel that is important for cyclic amp-stimulated intestinal secretion of chloride io TISSUE:abondantly expressed in heart, pancreas, prostate, kidney, small intestine and peripheral blood

leukocytes. less abundant in placenta, lung, spleen, colon, thymus, testis and ovaries. Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNQ1. The function of KCNQ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM339.ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM1025 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31088, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37782] Another function of VGAM1025 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. Chromosome 20 Open

Reading Frame 13 (C20orf13, Accession NM_017714) is another VGAM1025 host target gene. C20orf13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf13 BINDING SITE, designated SEQ ID:19301, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37783] Another function of VGAM1025 is therefore inhibition of Chromosome 20 Open Reading Frame 13 (C20orf13, Accession NM_017714). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf13. DKFZp566H0824 (Accession NM_017535) is another VGAM1025 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated

SEQ ID:18976, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37784] Another function of VGAM1025 is therefore inhibition of DKFZp566H0824 (Accession NM_017535). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. IMPACT (Accession NM_018439) is another VGAM1025 host target gene. IMPACT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPACT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPACT BINDING SITE, designated SEQ ID:20506, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37785] Another function of VGAM1025 is therefore inhibition of IMPACT (Accession NM_018439). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPACT. KIAA0010 (Accession NM_014671) is another VGAM1025 host target gene. KIAA0010 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0010 BINDING SITE, designated SEQ ID:16132, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37786] Another function of VGAM1025 is therefore inhibition of KIAA0010 (Accession NM_014671). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0010. KIAA0978 (Accession XM_047013) is another VGAM1025 host target gene. KIAA0978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0978, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0978 BINDING SITE, designated SEQ ID:34890, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37787] Another function of VGAM1025 is therefore inhibition of

KIAA0978 (Accession XM_047013). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0978. KIAA1550 (Accession XM_039393) is another VGAM1025 host target gene. KIAA1550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1550 BINDING SITE, designated SEQ ID:33072, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37788] Another function of VGAM1025 is therefore inhibition of KIAA1550 (Accession XM_039393). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1550. LOC157918 (Accession XM_098842) is another VGAM1025 host target gene. LOC157918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC157918 BINDING SITE, designated SEQ ID:41900, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37789] Another function of VGAM1025 is therefore inhibition of LOC157918 (Accession XM_098842). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157918. LOC202347 (Accession XM_117390) is another VGAM1025 host target gene. LOC202347 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202347 BINDING SITE, designated SEQ ID:43432, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37790] Another function of VGAM1025 is therefore inhibition of LOC202347 (Accession XM_117390). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202347. LOC203504 (Accession XM_117550) is an-

other VGAM1025 host target gene. LOC203504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203504 BINDING SITE, designated SEQ ID:43574, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37791] Another function of VGAM1025 is therefore inhibition of LOC203504 (Accession XM_117550). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203504. LOC257159 (Accession XM_173158) is another VGAM1025 host target gene. LOC257159 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257159 BINDING SITE, designated SEQ ID:46417, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37792] Another function of VGAM1025 is therefore inhibition of LOC257159 (Accession XM_173158). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257159. LOC89919 (Accession XM_027244) is another VGAM1025 host target gene. LOC89919 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89919 BINDING SITE, designated SEQ ID:30466, to the nucleotide sequence of VGAM1025 RNA, herein designated VGAM RNA, also designated SEQ ID:3736.

[37793] Another function of VGAM1025 is therefore inhibition of LOC89919 (Accession XM_027244). Accordingly, utilities of VGAM1025 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89919. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1026 (VGAM1026) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[37794] VGAM1026 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1026 was detected is described hereinabove with reference to Figs. 1–8.

[37795] VGAM1026 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cereal Yellow Dwarf Virus – RPV. VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37796] VGAM1026 gene encodes a VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1026 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1026 precursor RNA is designated SEQ ID:1012, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1012 is located at position 1766 relative to the genome of Cereal Yellow Dwarf Virus – RPV.

[37797] VGAM1026 precursor RNA folds onto itself, forming VGAM1026 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37798] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1026 folded precursor RNA into VGAM1026 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1026 RNA is designated SEQ ID:3737, and is provided hereinbelow with reference to the sequence listing part.

[37799] VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1026 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37800] VGAM1026 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1026 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1026 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37801] The complementary binding of VGAM1026 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1026 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1026 host target RNA into VGAM1026 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37802] It is appreciated that VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1026 host target genes. The mRNA of each one of this plurality of VGAM1026 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1026 RNA, herein designated VGAM RNA, and which when bound by VGAM1026 RNA causes inhibition of translation of respective one or more VGAM1026 host target proteins.

[37803] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1026 gene, herein designated VGAM GENE, on one or more VGAM1026 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37804] It is yet further appreciated that a function of VGAM1026 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGAM1026 correlate with, and may be deduced from, the identity of the host target genes which VGAM1026 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[37805] Nucleotide sequences of the VGAM1026 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1026 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1026 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1026 are further described hereinbelow with reference to Table 1.

[37806] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1026 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1026 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37807] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1026 gene, herein designated VGAM is inhibition of expression of VGAM1026 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1026 correlate with, and may be deduced from, the identity of the target genes which VGAM1026 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37808] CERD4 (Accession NM_012074) is a VGAM1026 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14349, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37809] A function of VGAM1026 is therefore inhibition of CERD4 (Accession NM_012074). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM_024009) is another VGAM1026 host target gene. GJB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GJB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJB3 BINDING SITE, designated SEQ ID:23438, to the nucleotide sequence of VGAM1026 RNA, herein

designated VGAM RNA, also designated SEQ ID:3737.

[37810] Another function of VGAM1026 is therefore inhibition of Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM_024009). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJB3. Kinesin Family Member 1B (KIF1B, Accession NM_015074) is another VGAM1026 host target gene. KIF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF1B BINDING SITE, designated SEQ ID:17449, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37811] Another function of VGAM1026 is therefore inhibition of Kinesin Family Member 1B (KIF1B, Accession NM_015074), a gene which motor for anterograde transport of mitochondria. has a microtubule plus end-directed motility. Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF1B. The function of KIF1B has

been established by previous studies. Nangaku et al. (1994) cloned a member of the mouse kinesin superfamily, Kif1b, which encodes an N-terminal-type motor protein. Kif1b was expressed in all tissues tested. In situ hybridization revealed that Kif1b is expressed abundantly in differentiated nerve cells. The authors found that Kif1b works as a monomer, having a microtubule plus-end-directed motility. Rotary shadowing electron microscopy revealed mostly single globular structures. Immunocytochemically, Kif1b was colocalized with mitochondria in vivo. A subcellular fractionation study showed that Kif1b is concentrated in the mitochondrial fraction, and purified Kif1b could transport mitochondria along microtubules in vitro. These data suggested that Kif1b works as a monomeric motor for anterograde transport of mitochondria. Zhao et al. (2001) identified an isoform of mouse Kif1b, which they called Kif1b-beta, that is distinct from Kif1b-alpha (Nangaku et al., 1994) in its cargo-binding domain. Yang et al. (2001) identified the KIF1B gene in a homozygously deleted region of chromosome 1p36.2 in a neuroblastoma cell line. They reported results suggesting that the gene is not a candidate for tumor suppressor gene of neuroblastoma. Northern blot analysis

demonstrated that human KIF1B has at least 2 isoforms. The long isoform (KIF1B-beta) was expressed in a wide variety of tissues, while the short isoform (KIF1B-alpha) was detected only in adult testis.

[37812] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37813] Yang, H. W.; Chen, Y. Z.; Takita, J.; Soeda, E.; Piao, H. Y.; Hayashi, Y. : Genomic structure and mutational analysis of the human KIF1B gene which is homozygously deleted in neuroblastoma at chromosome 1p36.2. Oncogene 20: 5075-5083, 2001. ; and

[37814] Nangaku, M.; Sato-Yoshitake, R.; Okada, Y.; Noda, Y.; Takemura, R.; Yamazaki, H.; Hirokawa, N. : KIF1B, a novel microtubule plus end-directed monomeric motor protein for transport of mi.

[37815] Further studies establishing the function and utilities of KIF1B are found in John Hopkins OMIM database record ID 605995, and in cited publications numbered 4431-443 and 2276 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237) is another VGAM1026 host target gene.

POU4F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU4F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU4F1 BINDING SITE, designated SEQ ID:12897, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37816] Another function of VGAM1026 is therefore inhibition of POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237), a gene which plays a role in the regulation of specific gene expression within a subset of neuronal lineages. Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU4F1. The function of POU4F1 has been established by previous studies. BRN3A (OMIM Ref. No. POU4F1) is a class IV POU domain-containing transcription factor highly expressed in the developing sensory nervous system and in cells of the B- and T-lymphocytic lineages (Gerrero et al., 1993). Xiang et al. (1995) analyzed the expression patterns of brn3a, brn3b, and brn3c in fetal and adult mouse retina and

brain. Antibodies to brn3a identify a large fraction of retinal ganglion cells. The 3 factors identify overlapping subsets of retinal ganglion cells and of neurons in the dorsal root and trigeminal ganglia, suggesting that primary somatosensory neurons and retinal ganglion cells share genetic regulatory hierarchies.

[37817] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37818] Gerrero, M. R.; McEvilly, R. J.; Turner, E.; Lin, C. R.; O'Connell, S.; Jenne, K. J.; Hobbs, M. V.; Rosenfeld, M. G. : Brn-3.0: a POU-domain protein expressed in the sensory immune and endocrine systems that functions on elements distinct from known octamer motifs. Proc. Nat. Acad. Sci. 90: 10841-10845, 1993. ; and

[37819] Xiang, M.; Zhou, L.; Macke, J. P.; Yoshioka, T.; Hendry, S. H. C.; Eddy, R. L.; Shows, T. B.; Nathans, J. : The Brn-3 family of POU-domain factors: primary structure, binding specificity, a.

[37820] Further studies establishing the function and utilities of POU4F1 are found in John Hopkins OMIM database record ID 601632, and in cited publications numbered 2805-2806, 2018, 280 and 3699 listed in the bibliogra-

phy section hereinbelow, which are also hereby incorporated by reference. BCL2/adenovirus E1B 19kDa Interacting Protein 2 (BNIP2, Accession XM_039703) is another VGAM1026 host target gene. BNIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BNIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNIP2 BINDING SITE, designated SEQ ID:33163, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37821] Another function of VGAM1026 is therefore inhibition of BCL2/adenovirus E1B 19kDa Interacting Protein 2 (BNIP2, Accession XM_039703). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNIP2. Chromosome 20 Open Reading Frame 173 (C20orf173, Accession NM_080828) is another VGAM1026 host target gene. C20orf173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf173 BINDING SITE, designated SEQ ID:28092, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37822] Another function of VGAM1026 is therefore inhibition of Chromosome 20 Open Reading Frame 173 (C20orf173, Accession NM_080828). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf173. DJ122O8.2 (Accession NM_020466) is another VGAM1026 host target gene. DJ122O8.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ122O8.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ122O8.2 BINDING SITE, designated SEQ ID:21704, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37823] Another function of VGAM1026 is therefore inhibition of DJ122O8.2 (Accession NM_020466). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DJ122O8.2. DKFZp547A023 (Accession XM_052065) is another VGAM1026 host target gene. DKFZp547A023 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp547A023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547A023 BINDING SITE, designated SEQ ID:35941, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37824] Another function of VGAM1026 is therefore inhibition of DKFZp547A023 (Accession XM_052065). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547A023. FLJ10607 (Accession XM_085119) is another VGAM1026 host target gene. FLJ10607 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ10607 BINDING SITE, designated SEQ ID:37833, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37825] Another function of VGAM1026 is therefore inhibition of FLJ10607 (Accession XM_085119). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10607. FLJ22795 (Accession NM_025084) is another VGAM1026 host target gene. FLJ22795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22795 BINDING SITE, designated SEQ ID:24689, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37826] Another function of VGAM1026 is therefore inhibition of FLJ22795 (Accession NM_025084). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22795. Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903) is another VGAM1026

host target gene. GABBR1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GABBR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABBR1 BINDING SITE, designated SEQ ID:22419, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37827] Another function of VGAM1026 is therefore inhibition of Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABBR1. KIAA0377 (Accession NM_014659) is another VGAM1026 host target gene. KIAA0377 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0377, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0377 BINDING SITE, designated SEQ ID:16102, to the nucleotide sequence of VGAM1026 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3737.

[37828] Another function of VGAM1026 is therefore inhibition of KIAA0377 (Accession NM_014659). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0377. KIAA0546 (Accession XM_049055) is another VGAM1026 host target gene. KIAA0546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0546 BINDING SITE, designated SEQ ID:35334, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37829] Another function of VGAM1026 is therefore inhibition of KIAA0546 (Accession XM_049055). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0546. KIAA1348 (Accession XM_043826) is another VGAM1026 host target gene. KIAA1348 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1348, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1348 BINDING SITE, designated SEQ ID:34033, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37830] Another function of VGAM1026 is therefore inhibition of KIAA1348 (Accession XM_043826). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1348. KIAA1706 (Accession XM_166595) is another VGAM1026 host target gene. KIAA1706 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1706 BINDING SITE, designated SEQ ID:44574, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37831] Another function of VGAM1026 is therefore inhibition of KIAA1706 (Accession XM_166595). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1706. RNP24 (Accession NM_006815) is another VGAM1026 host target gene. RNP24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNP24 BINDING SITE, designated SEQ ID:13692, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37832] Another function of VGAM1026 is therefore inhibition of RNP24 (Accession NM_006815). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNP24. LOC145717 (Accession XM_039771) is another VGAM1026 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33192, to

the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37833] Another function of VGAM1026 is therefore inhibition of LOC145717 (Accession XM_039771). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC145725 (Accession XM_085211) is another VGAM1026 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37948, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37834] Another function of VGAM1026 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM1026 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37957, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37835] Another function of VGAM1026 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC196957 (Accession XM_113789) is another VGAM1026 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42429, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37836] Another function of VGAM1026 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities

of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196957. LOC196961 (Accession XM_113790) is another VGAM1026 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42438, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37837] Another function of VGAM1026 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM1026 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC197138 BINDING SITE, designated SEQ ID:42456, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37838] Another function of VGAM1026 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC220537 (Accession XM_165406) is another VGAM1026 host target gene. LOC220537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220537 BINDING SITE, designated SEQ ID:43622, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37839] Another function of VGAM1026 is therefore inhibition of LOC220537 (Accession XM_165406). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220537. LOC245727 (Accession XM_165913) is another VGAM1026 host target gene. LOC245727 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245727 BINDING SITE, designated SEQ ID:43797, to the nucleotide sequence of VGAM1026 RNA, herein designated VGAM RNA, also designated SEQ ID:3737.

[37840] Another function of VGAM1026 is therefore inhibition of LOC245727 (Accession XM_165913). Accordingly, utilities of VGAM1026 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245727. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1027 (VGAM1027) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37841] VGAM1027 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1027 was detected is described hereinabove with reference to Figs. 1-8.

[37842] VGAM1027 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid Herpesvirus 1. VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37843] VGAM1027 gene encodes a VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1027 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1027 precursor RNA is designated SEQ ID:1013, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1013 is located at position 89420 relative to the genome of Ictalurid Herpesvirus 1.

[37844] VGAM1027 precursor RNA folds onto itself, forming VGAM1027 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[37845] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1027 folded precursor RNA into VGAM1027 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1027 RNA is designated SEQ ID:3738, and is provided hereinbelow with reference to the sequence listing part.

[37846] VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1027 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37847] VGAM1027 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1027 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1027 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1027 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37848] The complementary binding of VGAM1027 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1027 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1027 host target RNA into VGAM1027 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37849] It is appreciated that VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1027 host target genes. The mRNA of each one of this plurality of VGAM1027 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1027 RNA, herein designated VGAM RNA, and which when bound by VGAM1027 RNA causes inhibition of translation of respective one or more VGAM1027 host target proteins.

[37850] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1027 gene, herein designated VGAM GENE, on one or more VGAM1027 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37851] It is yet further appreciated that a function of VGAM1027 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of viral infection by Ictalurid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1027 correlate with, and may be deduced from, the identity of the host target genes which VGAM1027 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37852] Nucleotide sequences of the VGAM1027 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1027 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1027 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1027 are further described hereinbelow with reference to Table 1.

[37853] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1027 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1027 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37854] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1027 gene, herein designated VGAM is inhibition of expression of VGAM1027 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1027 correlate with, and may be deduced from, the identity of the target genes which VGAM1027 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37855] BarH-like Homeobox 1 (BARX1, Accession NM_021570) is a VGAM1027 host target gene. BARX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BARX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of BARX1 BINDING SITE, designated SEQ ID:22236, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37856] A function of VGAM1027 is therefore inhibition of BarH-like Homeobox 1 (BARX1, Accession NM_021570), a gene which involves in craniofacial development, in odontogenesis and in stomach organogenesis. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BARX1. The function of BARX1 has been established by previous studies. Using the mouse Barx1 sequence to search sequence databases, followed by PCR screening of cDNA libraries, Gould and Walter (2000) isolated a cDNA encoding human BARX1. The predicted 226-amino acid protein is identical in the homeodomain to the mouse and chick sequences and is approximately 90% identical overall. Northern blot analysis detected expression of a 1.6-kb transcript, with highest expression in testis and heart and lower levels in other tissues. Genomic sequence analysis determined that the BARX1 gene contains 4 exons. Animal model experiments lend further support to the function of BARX1. In a series of expression studies in mouse, Tucker

et al. (1998) demonstrated that bone morphogenetic protein-4 (Bmp4) activates the expression of Msx1 (OMIM Ref. No. 142983), leading to incisor tooth development. BMP4 inhibited expression of Barx1, which marks presumptive molar teeth, and limits expression to the proximal, presumptive molar mesenchyme at embryonic day 10. Fibroblast growth factor-8 (FGF8; 600483) stimulated Barx1 expression. When BMP4 signaling in early development was inhibited by application of exogenous Noggin (OMIM Ref. No. 602991) protein, ectopic Barx1 expression resulted in transformation of tooth identity from incisor to molar

[37857] It is appreciated that the abovementioned animal model for BARX1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[37858] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37859] Gould, D. B.; Walter, M. A. : Cloning, characterization, localization, and mutational screening of the human BARX1 gene. Genomics 68: 336-342, 2000. ; and

[37860] Tucker, A. S.; Matthews, K. L.; Sharpe, P. T. : Transforma-

tion of tooth type induced by inhibition of BMP signaling. Science 282: 1136–1138, 1998.

[37861] Further studies establishing the function and utilities of BARX1 are found in John Hopkins OMIM database record ID 603260, and in cited publications numbered 8739–874 and 11637 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Forkhead Box E3 (FOXE3, Accession NM_012186) is another VGAM1027 host target gene. FOXE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXE3 BINDING SITE, designated SEQ ID:14469, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37862] Another function of VGAM1027 is therefore inhibition of Forkhead Box E3 (FOXE3, Accession NM_012186), a gene which regulates embryonic development. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXE3. The function of FOXE3 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM632. Glucose-6-phosphate Dehydrogenase (G6PD, Accession NM_000402) is another VGAM1027 host target gene. G6PD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by G6PD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PD BINDING SITE, designated SEQ ID:5979, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37863] Another function of VGAM1027 is therefore inhibition of Glucose-6-phosphate Dehydrogenase (G6PD, Accession NM_000402), a gene which produces pentose sugars for nucleic acid synthesis and main producer of nadph reducing power. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PD. The function of G6PD has been established by previous studies. Since identification of deficiency of G6PD (Carson et al., 1956) and of its X-chromosomal determination (Childs et al., 1958) in the

1950s and demonstration of electrophoretic variants of this enzyme in the early 1960s (Boyer et al., 1962), the genetic, clinical and biochemical significance of this polymorphism has been found to be great. G6PD is in the hexose monophosphate pathway, the only NADPH-generation process in mature red cells, which lack the citric acid cycle. For this reason G6PD deficiency has adverse physiologic effects. Deficiency of the red cell enzyme, in various forms, is the basis of favism, primaquine sensitivity and some other drug-sensitive hemolytic anemias, anemia and jaundice in the newborn, and chronic nonspherocytic hemolytic anemia (Beutler et al., 1968). Beaconsfield et al. (1965) advanced the hypothesis that the incidence of cancer is inversely related to the frequency of G6PD deficiency in blacks. Since the metabolism of xylitol remains intact in G6PD-dependent red cells, Wang et al. (1971) suggested use of xylitol in the treatment of hemolytic crisis. Different variants of the enzyme are found in high frequency in African, Mediterranean and Asiatic populations (Porter et al., 1964), and heterozygote advantage vis-a-vis malaria (Luzzatto et al., 1969) has been invoked to account for the high frequency of the particular alleles in particular populations. The variety of

forms of the enzyme is great, as illustrated by the published tables (Yoshida et al., 1971; Beutler and Yoshida, 1973; Yoshida and Beutler, 1978) and by the listing of allelic variants in this entry. The World Health Organization (363,364:WHO, 1967,1967) gave its attention to problems of nomenclature and standard procedures for study. The demonstrated polymorphism at this X-linked locus rivals that of the autosomal loci for the polypeptide chains of hemoglobin. As in the latter instance, single amino acid substitution has been demonstrated as the basis of the change in the G6PD molecule resulting from mutation (Yoshida et al., 1967). Polymorphism at the G6PD locus has made it a useful X-chromosome marker, like the colorblindness and Xg blood group loci; close linkage of the colorblindness loci, the G6PD locus, and the hemophilia A locus (Adam et al., 1966; Boyer and Graham, 1965) has been demonstrated. Also, as a biochemical phenotype identifiable at the cellular level, G6PD variants have been useful in somatic cell genetics, permitting, for example, one of the critical proofs in man of the Lyon hypothesis (Davidson et al., 1963). The relative stability of the X chromosome during evolution has been shown by the fact that the G6PD locus is X-borne also in a number of other

species (Ohno, 1967). That G6PD is X-linked in the mouse is supported by Epstein's finding (1969) that oocytes of XO females have half as much G6PD as do oocytes of XX female mice. The level of lactate dehydrogenase was the same. Epstein's conclusion was that the G6PD gene is X-linked in the mouse, that synthesis occurs in the oocyte and is dosage-dependent, and that X-inactivation does not occur in oocytes. G6PD and HPRT are linked in the Chinese hamster (Rosenstrauss and Chasin, 1975) and presumably are on the X chromosome as in man. By study of cell hybrids, Shows et al. (1976) found that HPRT and G6PD are closely linked in the Muntjac deer. Smith et al. (1976) found G6PD deficiency in a male Weimaraner dog, but were not able to do genetic studies. Alpha-GAL, HPRT, PGK and G6PD are X-linked in the rabbit, according to mouse-rabbit hybrid cell studies (Cianfriglia et al., 1979; Echard and Gillois, 1979). By comparable methods, Hors-Cayla et al. (1979) found them to be X-linked also in cattle. According to cell hybridization studies, HPRT, G6PD, and PGK are X-linked in the pig (Gellin et al., 1979) and in sheep (Saidi et al., 1979). Pretsch et al. (1988) recovered a mouse with X-linked G6PD deficiency from the offspring of 1-ethyl-1-nitrosourea-treated male mice. Using pulsed

field gel electrophoresis, Faust et al. (1992) demonstrated that, in the mouse, Gdx (OMIM Ref. No. 312070), P3 (OMIM Ref. No. 312090), and G6pd are physically linked to the X-linked visual pigment locus (Rsvp) within a maximal distance of 340 kb, while G6pd and Cf-8 (OMIM Ref. No. 306700) are approximately 900 kb apart.

[37864] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37865] Beutler, E.; Mathai, C. K.; Smith, J. E. : Biochemical variants of glucose-6-phosphate dehydrogenase giving rise to congenital nonspherocytic hemolytic disease. Blood 31: 131-150, 1968. ; and

[37866] Wang, Y. M.; Patterson, J. H.; Van Eys, J. : The potential use of xylitol in glucose-6-phosphate dehydrogenase deficiency anemia. J. Clin. Invest. 50: 1421-1428, 1971.

[37867] Further studies establishing the function and utilities of G6PD are found in John Hopkins OMIM database record ID 305900, and in cited publications numbered 11064-11075, 4212, 8019-8055, 8676-8678, 7352, 8679-8691, 8804-870 and 8258-8276 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate-cysteine Ligase, Modifier

Subunit (GCLM, Accession NM_002061) is another VGAM1027 host target gene. GCLM BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GCLM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCLM BINDING SITE, designated SEQ ID:7821, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37868] Another function of VGAM1027 is therefore inhibition of Glutamate-cysteine Ligase, Modifier Subunit (GCLM, Accession NM_002061), a gene which is GLUTAMATE-CYSTEINE LIGASE. Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCLM. The function of GCLM has been established by previous studies. Gamma-glutamylcysteine synthetase, also known as glutamate-cysteine ligase (EC 6.3.2.2), is the first rate-limiting enzyme in glutathione biosynthesis.

[37869] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37870] Gipp, J. J.; Bailey, H. H.; Mulcahy, R. T. : Cloning and sequencing of the cDNA for the light subunit of human liver gamma-glutamylcysteine synthetase and relative mRNA levels for heavy and light subunits in human normal tissues. *Biochem. Biophys. Res. Commun.* 206: 584–589, 1995. ; and

[37871] Tsuchiya, K.; Mulcahy, R. T.; Reid, L. L.; Disteché, C. M.; Kavanagh, T. J. : Mapping of the glutamate-cysteine ligase catalytic subunit gene (GLCLC) to human chromosome 6p12 and mouse c.

[37872] Further studies establishing the function and utilities of GCLM are found in John Hopkins OMIM database record ID 601176, and in cited publications numbered 9314–931 and 9320–9317 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Ret Finger Protein (RFP, Accession NM_006510) is another VGAM1027 host target gene. RFP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RFP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFP BINDING SITE, designated SEQ ID:13258, to the nucleotide sequence of

VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37873] Another function of VGAM1027 is therefore inhibition of Ret Finger Protein (RFP, Accession NM_006510), a gene which involves in transcriptional regulation and may act in male germ cell development . Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFP. The function of RFP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM302.SORCS2 (Accession NM_020777) is another VGAM1027 host target gene. SORCS2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SORCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS2 BINDING SITE, designated SEQ ID:21877, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37874] Another function of VGAM1027 is therefore inhibition of SORCS2 (Accession NM_020777). Accordingly, utilities of

VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS2. Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575) is another VGAM1027 host target gene. C17orf31 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:19003, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37875] Another function of VGAM1027 is therefore inhibition of Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf31. Centaurin, Gamma 2 (CENTG2, Accession NM_014914) is another VGAM1027 host target gene. CENTG2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CENTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG2 BINDING SITE, designated SEQ ID:17158, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37876] Another function of VGAM1027 is therefore inhibition of Centaurin, Gamma 2 (CENTG2, Accession NM_014914). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG2. DT1P1A10 (Accession XM_029187) is another VGAM1027 host target gene. DT1P1A10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DT1P1A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DT1P1A10 BINDING SITE, designated SEQ ID:30858, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37877] Another function of VGAM1027 is therefore inhibition of DT1P1A10 (Accession XM_029187). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DT1P1A10. E2IG3 (Accession NM_014366) is another VGAM1027 host target gene. E2IG3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by E2IG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2IG3 BINDING SITE, designated SEQ ID:15696, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37878] Another function of VGAM1027 is therefore inhibition of E2IG3 (Accession NM_014366). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2IG3. Epsin 2 (EPN2, Accession NM_014964) is another VGAM1027 host target gene. EPN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EPN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPN2 BINDING SITE, designated SEQ ID:17347, to the nucleotide sequence of

VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37879] Another function of VGAM1027 is therefore inhibition of Epsin 2 (EPN2, Accession NM_014964). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPN2. FLJ20400 (Accession XM_039306) is another VGAM1027 host target gene. FLJ20400 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20400 BINDING SITE, designated SEQ ID:33045, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37880] Another function of VGAM1027 is therefore inhibition of FLJ20400 (Accession XM_039306). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20400. FLJ20979 (Accession NM_024121) is another VGAM1027 host target gene. FLJ20979 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by FLJ20979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20979 BINDING SITE, designated SEQ ID:23573, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37881] Another function of VGAM1027 is therefore inhibition of FLJ20979 (Accession NM_024121). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20979. FLJ21195 (Accession NM_022469) is another VGAM1027 host target gene. FLJ21195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21195 BINDING SITE, designated SEQ ID:22826, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37882] Another function of VGAM1027 is therefore inhibition of FLJ21195 (Accession NM_022469). Accordingly, utilities of

VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21195. FLJ21562 (Accession NM_025113) is another VGAM1027 host target gene. FLJ21562 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ21562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21562 BINDING SITE, designated SEQ ID:24762, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37883] Another function of VGAM1027 is therefore inhibition of FLJ21562 (Accession NM_025113). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21562. KIAA0415 (Accession XM_166527) is another VGAM1027 host target gene. KIAA0415 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0415 BINDING SITE, designated SEQ ID:44476, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37884] Another function of VGAM1027 is therefore inhibition of KIAA0415 (Accession XM_166527). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0415. KIAA0683 (Accession NM_016111) is another VGAM1027 host target gene. KIAA0683 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0683, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0683 BINDING SITE, designated SEQ ID:18191, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37885] Another function of VGAM1027 is therefore inhibition of KIAA0683 (Accession NM_016111). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0683. KIAA1643 (Accession XM_035371) is another VGAM1027 host target gene. KIAA1643 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1643 BINDING SITE, designated SEQ ID:32240, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37886] Another function of VGAM1027 is therefore inhibition of KIAA1643 (Accession XM_035371). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1643. MGC10986 (Accession NM_030576) is another VGAM1027 host target gene. MGC10986 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10986 BINDING SITE, designated SEQ ID:24950, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37887] Another function of VGAM1027 is therefore inhibition of

MGC10986 (Accession NM_030576). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10986. Phosphatidylserine Synthase 2 (PTDSS2, Accession NM_030783) is another VGAM1027 host target gene. PTDSS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTDSS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTDSS2 BINDING SITE, designated SEQ ID:25075, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37888] Another function of VGAM1027 is therefore inhibition of Phosphatidylserine Synthase 2 (PTDSS2, Accession NM_030783). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTDSS2. LOC254057 (Accession XM_173085) is another VGAM1027 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254057, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254057 BINDING SITE, designated SEQ ID:46344, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37889] Another function of VGAM1027 is therefore inhibition of LOC254057 (Accession XM_173085). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254057. LOC254528 (Accession XM_170797) is another VGAM1027 host target gene. LOC254528 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254528 BINDING SITE, designated SEQ ID:45567, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37890] Another function of VGAM1027 is therefore inhibition of LOC254528 (Accession XM_170797). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC254528. LOC257479 (Accession XM_171548) is another VGAM1027 host target gene. LOC257479 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257479 BINDING SITE, designated SEQ ID:46052, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37891] Another function of VGAM1027 is therefore inhibition of LOC257479 (Accession XM_171548). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257479. LOC56926 (Accession XM_052629) is another VGAM1027 host target gene. LOC56926 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC56926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56926 BINDING SITE, designated SEQ ID:36042, to the

nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37892] Another function of VGAM1027 is therefore inhibition of LOC56926 (Accession XM_052629). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56926. LOC56961 (Accession XM_031857) is another VGAM1027 host target gene. LOC56961 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56961 BINDING SITE, designated SEQ ID:31507, to the nucleotide sequence of VGAM1027 RNA, herein designated VGAM RNA, also designated SEQ ID:3738.

[37893] Another function of VGAM1027 is therefore inhibition of LOC56961 (Accession XM_031857). Accordingly, utilities of VGAM1027 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56961. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1028 (VGAM1028) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37894] VGAM1028 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1028 was detected is described hereinabove with reference to Figs. 1–8.

[37895] VGAM1028 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid Herpesvirus 1. VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37896] VGAM1028 gene encodes a VGAM1028 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1028 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1028 precursor RNA is designated SEQ ID:1014, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1014 is located at position 86483 relative to the genome of Ictalurid Herpesvirus 1.

[37897] VGAM1028 precursor RNA folds onto itself, forming VGAM1028 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37898] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1028 folded precursor RNA into VGAM1028 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1028 RNA is designated SEQ ID:3739, and is provided hereinbelow with reference to the sequence listing part.

[37899] VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1028 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1028 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[37900] VGAM1028 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1028 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1028 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37901] The complementary binding of VGAM1028 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1028 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1028 host target RNA into VGAM1028 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37902] It is appreciated that VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1028 host target genes. The mRNA of each one of this plurality of VGAM1028 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1028 RNA, herein designated VGAM RNA, and which when bound by VGAM1028 RNA causes inhibition of translation of respective one or more VGAM1028 host target proteins.

[37903] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1028 gene, herein designated VGAM GENE, on one or more VGAM1028 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37904] It is yet further appreciated that a function of VGAM1028 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of viral infection by Ictalurid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1028 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1028 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37905] Nucleotide sequences of the VGAM1028 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1028 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1028 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1028 are further described hereinbelow with reference to Table 1.

[37906] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1028 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1028 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37907] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1028 gene, herein designated VGAM is inhibition of expression of VGAM1028 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1028 correlate with, and may be deduced from, the identity of the target genes which VGAM1028

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37908] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974) is a VGAM1028 host target gene. AKAP13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:43174, to the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, also designated SEQ ID:3739.

[37909] A function of VGAM1028 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17.DKFZP434N014 (Accession XM_027012) is another VGAM1028 host target gene. DK-

FZP434N014 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434N014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N014 BINDING SITE, designated SEQ ID:30388, to the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, also designated SEQ ID:3739.

[37910] Another function of VGAM1028 is therefore inhibition of DKFZP434N014 (Accession XM_027012). Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N014. FLJ23598 (Accession NM_024783) is another VGAM1028 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24152, to the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, also designated SEQ ID:3739.

[37911] Another function of VGAM1028 is therefore inhibition of FLJ23598 (Accession NM_024783). Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. LOC149086 (Accession XM_097580) is another VGAM1028 host target gene. LOC149086 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149086 BINDING SITE, designated SEQ ID:40945, to the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, also designated SEQ ID:3739.

[37912] Another function of VGAM1028 is therefore inhibition of LOC149086 (Accession XM_097580). Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149086. LOC92568 (Accession XM_045852) is another VGAM1028 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34572, to the nucleotide sequence of VGAM1028 RNA, herein designated VGAM RNA, also designated SEQ ID:3739.

[37913] Another function of VGAM1028 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM1028 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1029 (VGAM1029) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37914] VGAM1029 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1029 was detected is described hereinabove with reference to Figs. 1–8.

[37915] VGAM1029 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Yellow Dwarf Virus – PAV. VGAM1029 host target gene, herein desig-

nated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37916] VGAM1029 gene encodes a VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1029 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1029 precursor RNA is designated SEQ ID:1015, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1015 is located at position 1469 relative to the genome of Barley Yellow Dwarf Virus – PAV.

[37917] VGAM1029 precursor RNA folds onto itself, forming VGAM1029 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37918] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1029 folded precursor RNA into VGAM1029

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1029 RNA is designated SEQ ID:3740, and is provided hereinbelow with reference to the sequence listing part.

[37919] VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1029 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37920] VGAM1029 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1029 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1029 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37921] The complementary binding of VGAM1029 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1029 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1029 host target RNA into VGAM1029 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[37922] It is appreciated that VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1029 host target genes. The mRNA of each one of this plurality of VGAM1029 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1029 RNA, herein designated VGAM RNA, and which when bound by VGAM1029 RNA causes inhibition of translation of respective one or more VGAM1029 host target proteins.

[37923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1029 gene, herein designated VGAM GENE, on one or more VGAM1029 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37924] It is yet further appreciated that a function of VGAM1029 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of viral infection by Barley Yellow Dwarf Virus – PAV. Specific functions, and accordingly utilities, of VGAM1029 correlate with, and may be deduced from, the identity of the host target genes which VGAM1029 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37925] Nucleotide sequences of the VGAM1029 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1029 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1029 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1029 are further described hereinbelow with reference to Table 1.

[37926] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1029 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1029 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37927] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1029 gene, herein designated VGAM is inhibition of expression of VGAM1029 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1029 correlate with, and may be deduced from, the identity of the target genes which VGAM1029 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37928] Glycine Receptor, Alpha 3 (GLRA3, Accession XM_011092) is a VGAM1029 host target gene. GLRA3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GLRA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLRA3 BINDING SITE, designated SEQ ID:30167, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA,

also designated SEQ ID:3740.

[37929] A function of VGAM1029 is therefore inhibition of Glycine Receptor, Alpha 3 (GLRA3, Accession XM_011092), a gene which increases the chloride conductance and thus produces hyperpolarization (inhibition of neuronal firing). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLRA3. The function of GLRA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM602.ATP-binding Cassette, Sub-family A (ABC1), Member 9 (ABCA9, Accession NM_080283) is another VGAM1029 host target gene. ABCA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA9 BINDING SITE, designated SEQ ID:27827, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37930] Another function of VGAM1029 is therefore inhibition of

ATP-binding Cassette, Sub-family A (ABC1), Member 9 (ABCA9, Accession NM_080283). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA9. Histamine Receptor H3 (HRH3, Accession NM_007232) is another VGAM1029 host target gene. HRH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH3 BINDING SITE, designated SEQ ID:14109, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37931] Another function of VGAM1029 is therefore inhibition of Histamine Receptor H3 (HRH3, Accession NM_007232). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH3. KIAA0892 (Accession XM_048457) is another VGAM1029 host target gene. KIAA0892 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0892, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0892 BINDING SITE, designated SEQ ID:35168, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37932] Another function of VGAM1029 is therefore inhibition of KIAA0892 (Accession XM_048457). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0892. KIAA1546 (Accession XM_042301) is another VGAM1029 host target gene. KIAA1546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1546 BINDING SITE, designated SEQ ID:33715, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37933] Another function of VGAM1029 is therefore inhibition of KIAA1546 (Accession XM_042301). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1546. LOC149832 (Accession XM_097733) is another VGAM1029 host target gene. LOC149832 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149832 BINDING SITE, designated SEQ ID:41079, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37934] Another function of VGAM1029 is therefore inhibition of LOC149832 (Accession XM_097733). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149832. LOC152274 (Accession XM_087418) is another VGAM1029 host target gene. LOC152274 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152274 BINDING SITE, designated SEQ ID:39234, to

the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37935] Another function of VGAM1029 is therefore inhibition of LOC152274 (Accession XM_087418). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152274. LOC157247 (Accession XM_088275) is another VGAM1029 host target gene. LOC157247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157247 BINDING SITE, designated SEQ ID:39571, to the nucleotide sequence of VGAM1029 RNA, herein designated VGAM RNA, also designated SEQ ID:3740.

[37936] Another function of VGAM1029 is therefore inhibition of LOC157247 (Accession XM_088275). Accordingly, utilities of VGAM1029 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157247. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1030 (VGAM1030) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[37937] VGAM1030 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1030 was detected is described hereinabove with reference to Figs. 1–8.

[37938] VGAM1030 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Mild Yellowing Virus. VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37939] VGAM1030 gene encodes a VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1030 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1030 precursor RNA is designated SEQ ID:1016, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1016 is located at position 3757 relative to the genome of Beet Mild Yellowing Virus.

[37940] VGAM1030 precursor RNA folds onto itself, forming VGAM1030 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37941] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1030 folded precursor RNA into VGAM1030 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1030 RNA is designated SEQ ID:3741, and is provided hereinbelow with reference to the sequence listing part.

[37942] VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1030 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1030 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37943] VGAM1030 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1030 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1030 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37944] The complementary binding of VGAM1030 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1030 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1030 host target RNA into VGAM1030 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37945] It is appreciated that VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1030 host target genes. The mRNA of each one of this plurality of VGAM1030 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1030 RNA, herein designated VGAM RNA, and which when bound by VGAM1030 RNA causes inhibition of translation of respective one or more VGAM1030 host target proteins.

[37946] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1030 gene, herein designated VGAM GENE, on one or more VGAM1030 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37947] It is yet further appreciated that a function of VGAM1030 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGAM1030 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1030 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[37948] Nucleotide sequences of the VGAM1030 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1030 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1030 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1030 are further described hereinbelow with reference to Table 1.

[37949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1030 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1030 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37950] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1030 gene, herein designated VGAM is inhibition of expression of VGAM1030 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1030 correlate with, and may be deduced from, the identity of the target genes which VGAM1030

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37951] Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM_000527) is a VGAM1030 host target gene. LDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LDLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDLR BINDING SITE, designated SEQ ID:6125, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37952] A function of VGAM1030 is therefore inhibition of Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM_000527), a gene which also acts as a tumor suppressor. Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDLR. The function of LDLR has been established by previous studies. The low density lipoprotein receptor is a cell surface receptor that plays an important role in cholesterol homeostasis. The low density lipoprotein receptor is syn-

thesized as a 120-kD glycoprotein precursor that undergoes change to a 160-kD mature glycoprotein through the covalent addition of a 40-kD protein (Tolleshaug et al., 1982). Yamamoto et al. (1984) reported that the human LDL receptor is an 839-amino acid protein rich in cysteine, with multiple copies of the Alu family of repetitive DNAs. Russell et al. (1984) demonstrated DNA sequence homology of the LDL receptor with the epidermal growth factor receptor (EGF; 131530). Francke et al. (1984) assigned the LDL receptor to chromosome 19 on the basis of expression studies in hamster-human somatic cell hybrids. The LDLR gene was regionalized to 19p13.1-p13.3 by in situ hybridization (Lindgren et al., 1985). Frank et al. (1989) identified RFLPs of the mouse LDL receptor gene and used them to map the gene, designated *Ldlr*, to the proximal region of chromosome 9. Using interspecific backcrosses, they established the order and interval distances for this and several other loci on mouse chromosome 9, namely, APOA4 (OMIM Ref. No. 107690), which is on chromosome 11 in man, and mannosephosphate isomerase (OMIM Ref. No. 154550), which is on chromosome 15 in man. In a patient with homozygous familial hypercholesterolemia (FH; 143890), Hobbs

et al. (1986) described an LDL receptor mutant in which 1 of the 7 repeating units constituting the ligand binding domain had been deleted. The deletion arose by homologous recombination by repetitive Alu sequences in intron 4 and intron 5 of the gene. The deletion removed exon 5, which normally encodes the sixth repeat of the ligand binding domain. In the resultant mRNA, exon 4 was found to be spliced to exon 6, preserving the reading frame. The resulting shortened protein reaches the cell surface and reacts with antireceptor antibodies but does not bind LDL. It does, however, bind VLDL, a lipoprotein that contains apoprotein E as well as apoprotein B-100. The findings in this instructive case support the hypothesis that the 7 repeated sequences in the receptor constitute the LDL binding domain, that the sixth repeat is required for binding of LDL but not of VLDL, and that deletion of a single repeat can alter the binding specificity of the LDL receptor. Horsthemke et al. (1987) analyzed DNA from 70 patients in the UK with heterozygous familial hypercholesterolemia. In most, the restriction fragment pattern of the LDLR gene was indistinguishable from the normal; however, 3 patients were found to have a deletion of about 1 kb in the central portion of the gene. In 2 patients, the

deletion included all or part of exon 5 (606945.0027); in the third, the deletion included exon 7 (606945.0033). Including a previously described patient with a deletion in the 3-prime part of the gene, these results indicated that 4 out of 70 patients, or 6%, have deletions. Langlois et al. (1988) screened 234 unrelated heterozygotes for FH to detect major rearrangements in the LDLR gene. Total genomic DNA was analyzed by Southern blot hybridization to probes encompassing exons 1 to 18 of the LDLR gene. Six different mutations were detected and characterized by use of exon-specific probes and detailed restriction mapping. The frequency of deletions in the Langlois et al. (1988) study was 2.5% (6 out of 234 patients). An illustration of previously mapped deletions and the deletions identified in this study (a total of 16) suggested that particular areas in the LDLR gene are susceptible to deletion. In a Japanese subject with homozygous hypercholesterolemia, Lehrman et al. (1987) found a 7.8-kb deletion in LDLR (606945.0029). The deletion joined intron 15 to the middle of exon 18, which encodes the 3-prime untranslated region, thereby removing all 3-prime splice acceptor sites distal to intron 15. The mRNA should produce a truncated receptor that lacks the normal membrane-

COOH terminus. Rudiger et al. (1991) reviewed previously described deletions in the LDLR gene in cases of familial hypercholesterolemia and reported the finding of a deletion in 3 of 25 unrelated patients with FH. Defesche and Kastelein (1998) stated that more than 350 different mutations had been found in patients with familial hypercholesterolemia. They tabulated the preferential geographic distribution that has been demonstrated for some of the LDL receptor mutations. For example, in the West of Scotland about half of the index cases of FH were found to have the cys163-to-tyr mutation (606945.0058). Defesche and Kastelein (1998) commented on the geographic associations of LDL receptor mutations within the Netherlands.

[37953] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37954] Durst, R.; Colombo, R.; Shpitzen, S.; Ben Avi, L.; Friedlander, Y.; Wexler, R.; Raal, F. J.; Marais, D. A.; Defesche, J. C.; Mandelshtam, M. Y.; Kotze, M. J.; Leitersdorf, E.; Meiner, V. : Recent origin and spread of a common Lithuanian mutation, G197del LDLR, causing familial hypercholesterolemia: positive selection is not always necessary to ac-

count for disease incidence among Ashkenazi Jews. Am. J. Hum. Genet. 68: 1172–1188, 2001. ; and

[37955] Rudiger, N. S.; Heinsvig, E. M.; Hansen, F. A.; Faergeman, O.; Bolund, L.; Gregersen, N. : DNA deletions in the low density lipoprotein (LDL) receptor gene in Danish families with fami.

[37956] Further studies establishing the function and utilities of LDLR are found in John Hopkins OMIM database record ID 606945, and in cited publications numbered 732–733, 5368–5373, 3029, 5374, 3032–3034, 5376–3037, 5141–3040, 5142–5144, 3897–3898, 5145–5149, 3899–3900, 5150–5152, 104, 3901–3902, 5153–5158, 3903–3906, 5505–5507, 3907–3908, 5508–5514, 3924, 5515–5525, 3614, 5568, 6088, 6089–6090, 3927, 6091–6100, 4958, 6101–6102, 392 and 6103 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Microtubule-associated Protein 1B (MAP1B, Accession NM_005909) is another VGAM1030 host target gene. MAP1B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com–

plementarity of the nucleotide sequences of MAP1B BINDING SITE, designated SEQ ID:12532, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37957] Another function of VGAM1030 is therefore inhibition of Microtubule-associated Protein 1B (MAP1B, Accession NM_005909), a gene which may have a role in neuronal plasticity and brain development. Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1B. The function of MAP1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM316. Arginyl Aminopeptidase (aminopeptidase B)-like 1 (RNPEPL1, Accession NM_018226) is another VGAM1030 host target gene. RNPEPL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNPEPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNPEPL1 BINDING SITE, designated SEQ ID:20158, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM

RNA, also designated SEQ ID:3741.

[37958] Another function of VGAM1030 is therefore inhibition of Arginyl Aminopeptidase (aminopeptidase B)-like 1 (RNPEPL1, Accession NM_018226). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNPEPL1. Von Hippel-Lindau Syndrome (VHL, Accession NM_000551) is another VGAM1030 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6158, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37959] Another function of VGAM1030 is therefore inhibition of Von Hippel-Lindau Syndrome (VHL, Accession NM_000551), a gene which may control rna stability through the selective degradation of rna-bound proteins. Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its as-

sociation with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM197.FLJ00007 (Accession XM_048928) is another VGAM1030 host target gene.

FLJ00007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00007 BINDING SITE, designated SEQ ID:35305, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37960] Another function of VGAM1030 is therefore inhibition of FLJ00007 (Accession XM_048928). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00007. FLJ10298 (Accession NM_018050) is another VGAM1030 host target gene. FLJ10298 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10298, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10298 BINDING SITE, designated SEQ ID:19807, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37961] Another function of VGAM1030 is therefore inhibition of FLJ10298 (Accession NM_018050). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10298. PRO1048 (Accession NM_018497) is another VGAM1030 host target gene. PRO1048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1048 BINDING SITE, designated SEQ ID:20556, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37962] Another function of VGAM1030 is therefore inhibition of PRO1048 (Accession NM_018497). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1048. LOC144108 (Accession XM_084736) is another

VGAM1030 host target gene. LOC144108 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144108 BINDING SITE, designated SEQ ID:37682, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37963] Another function of VGAM1030 is therefore inhibition of LOC144108 (Accession XM_084736). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144108. LOC152441 (Accession XM_098230) is another VGAM1030 host target gene. LOC152441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152441 BINDING SITE, designated SEQ ID:41504, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37964] Another function of VGAM1030 is therefore inhibition of LOC152441 (Accession XM_098230). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152441. LOC153688 (Accession XM_098416) is another VGAM1030 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41652, to the nucleotide sequence of VGAM1030 RNA, herein designated VGAM RNA, also designated SEQ ID:3741.

[37965] Another function of VGAM1030 is therefore inhibition of LOC153688 (Accession XM_098416). Accordingly, utilities of VGAM1030 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1031 (VGAM1031) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[37966] VGAM1031 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1031 was detected is described hereinabove with reference to Figs. 1-8.

[37967] VGAM1031 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Mild Yellowing Virus. VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[37968] VGAM1031 gene encodes a VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1031 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1031 precursor RNA is designated SEQ ID:1017, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1017 is located at position 2997 relative to the genome of Beet Mild Yellowing Virus.

[37969] VGAM1031 precursor RNA folds onto itself, forming VGAM1031 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[37970] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1031 folded precursor RNA into VGAM1031 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1031 RNA is designated SEQ ID:3742, and is provided hereinbelow with reference to the sequence listing part.

[37971] VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1031 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[37972] VGAM1031 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1031 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1031 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[37973] The complementary binding of VGAM1031 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1031 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1031 host target RNA into VGAM1031 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[37974] It is appreciated that VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1031 host target genes. The mRNA of each one of this plurality of VGAM1031 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1031 RNA, herein designated VGAM RNA, and which when bound by VGAM1031 RNA causes inhibition of translation of respective one or more VGAM1031 host target proteins.

[37975] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1031 gene, herein designated VGAM GENE, on one or more VGAM1031 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[37976] It is yet further appreciated that a function of VGAM1031 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1031 include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGAM1031 correlate with, and may be deduced from, the identity of the host target genes which VGAM1031 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[37977] Nucleotide sequences of the VGAM1031 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1031 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1031 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1031 are further described hereinbelow with reference to Table 1.

[37978] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1031 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1031 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[37979] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1031 gene, herein designated VGAM is inhibition of expression of VGAM1031 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1031 correlate with, and may be deduced from, the identity of the target genes which VGAM1031 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[37980] TAR (HIV) RNA Binding Protein 2 (TARBP2, Accession NM_134323) is a VGAM1031 host target gene. TARBP2 BINDING SITE1 and TARBP2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TARBP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TARBP2 BINDING SITE1 and TARBP2 BINDING SITE2, designated SEQ ID:28625 and SEQ ID:28627 respectively, to the nucleotide sequence of VGAM1031 RNA, herein designated VGAM RNA, also designated SEQ ID:3742.

[37981] A function of VGAM1031 is therefore inhibition of TAR (HIV) RNA Binding Protein 2 (TARBP2, Accession NM_134323), a gene which is involved in the regulation of HIV replication. Accordingly, utilities of VGAM1031 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TARBP2. The function of TARBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95.EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883) is another VGAM1032 host target gene.

EGFL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30966, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37982] Another function of VGAM1032 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL4. Galactosamine (N-acetyl)-6-sulfate Sulfatase (Morquio syndrome, mucopolysaccharidosis type IVA) (GALNS, Accession NM_000512) is another VGAM1032 host target gene. GALNS BINDING SITE1 and GALNS BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GALNS, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNS BINDING SITE1

and GALNS BINDING SITE2, designated SEQ ID:6123 and SEQ ID:6122 respectively, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37983] Another function of VGAM1032 is therefore inhibition of Galactosamine (N-acetyl)-6-sulfate Sulfatase (Morquio syndrome, mucopolysaccharidosis type IVA) (GALNS, Accession NM_000512). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNS. Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM_002309) is another VGAM1032 host target gene. LIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIF BINDING SITE, designated SEQ ID:8094, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37984] Another function of VGAM1032 is therefore inhibition of Leukemia Inhibitory Factor (cholinergic differentiation factor) (LIF, Accession NM_002309). Accordingly, utilities of

VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIF. Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926) is another VGAM1032 host target gene. MBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD3 BINDING SITE, designated SEQ ID:10019, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37985] Another function of VGAM1032 is therefore inhibition of Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926), a gene which are subunits of the NURD (nucleosome remodeling and histone deacetylase) complex. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD3. The function of MBD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Prospero-related Homeobox 1 (PROX1, Acces-

sion NM_002763) is another VGAM1032 host target gene. PROX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROX1 BINDING SITE, designated SEQ ID:8650, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37986] Another function of VGAM1032 is therefore inhibition of Prospero-related Homeobox 1 (PROX1, Accession NM_002763), a gene which may regulate gene expression and development of postmitotic undifferentiated young neurons. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROX1. The function of PROX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621) is another VGAM1032 host target gene. TRPC6 BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10973, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37987] Another function of VGAM1032 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349) is another VGAM1032 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3, designated SEQ ID:9371, SEQ ID:22523 and SEQ ID:22770 respectively, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37988] Another function of VGAM1032 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM155.YY1 Transcription Factor (YY1, Accession NM_003403) is another VGAM1032 host target gene. YY1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by YY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

YY1 BINDING SITE, designated SEQ ID:9437, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37989] Another function of VGAM1032 is therefore inhibition of YY1 Transcription Factor (YY1, Accession NM_003403), a gene which is involved in transcriptional regulation and may play an important role in development and differentiation. Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YY1. The function of YY1 has been established by previous studies. Functionally, YY1 is a versatile factor, being a negative regulator in some systems and a positive regulator in others. In some systems, the function of YY1 as an activator or a repressor is specified by the presence of other proteins. By site-directed mutagenesis and overexpression of YY1 in human fibroblasts, Yan et al. (2002) showed that YY1, as well as HRY (OMIM Ref. No. 139605), functions as a transcriptional activator of acid alpha-glucosidase (GAA; 232300). In previous studies, Yan et al. (2001) had found that YY1, binding to the same element of the GAA gene in hepatoma cells, acts as a GAA transcription silencer. Oei and Shi (2001) noted that physical interaction had been reported between

YY1 and poly(ADP-ribose) polymerase (PARP; 173870).

PARP is a nuclear enzyme that catalyzes the synthesis of ADP-ribose polymers from NAD⁺, a function related to DNA repair and transcription. Oei and Shi (2001) found that overexpression of YY1 in HeLa cells resulted in intracellular accumulation of poly(ADP-ribose) and acceleration of DNA repair following damage with genotoxic agents, suggesting a functional as well as physical interaction between the proteins.

[37990] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[37991] Oei, S. L.; Shi, Y. : Transcription factor Yin Yang 1 stimulates poly(ADP-ribosyl)ation and DNA repair. *Biochem. Biophys. Res. Commun.* 284: 450-454, 2001. ; and

[37992] Yan, B.; Raben, N.; Plotz, P. H. : Hes-1, a known transcriptional repressor, acts as a transcriptional activator for the human acid alpha-glucosidase gene in human fibroblast cells. *Bi.*

[37993] Further studies establishing the function and utilities of YY1 are found in John Hopkins OMIM database record ID 600013, and in cited publications numbered 8350-8354, 3574-357 and 8355-8356 listed in the bibliography sec-

tion hereinbelow, which are also hereby incorporated by reference. E46L (Accession NM_013236) is another VGAM1032 host target gene. E46L BINDING SITE1 and E46L BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by E46L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E46L BINDING SITE1 and E46L BINDING SITE2, designated SEQ ID:14896 and SEQ ID:14897 respectively, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37994] Another function of VGAM1032 is therefore inhibition of E46L (Accession NM_013236). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E46L. FLJ14249 (Accession NM_106552) is another VGAM1032 host target gene. FLJ14249 BINDING SITE1 and FLJ14249 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ14249, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of FLJ14249 BINDING SITE1 and FLJ14249 BINDING SITE2, designated SEQ ID:28169 and SEQ ID:23986 respectively, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37995] Another function of VGAM1032 is therefore inhibition of FLJ14249 (Accession NM_106552). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14249. KIAA0939 (Accession XM_030524) is another VGAM1032 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31061, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37996] Another function of VGAM1032 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. MGC13170 (Accession NM_032712) is another

VGAM1032 host target gene. MGC13170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13170 BINDING SITE, designated SEQ ID:26431, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37997] Another function of VGAM1032 is therefore inhibition of MGC13170 (Accession NM_032712). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13170. Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM_015879) is another VGAM1032 host target gene. SIAT8C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT8C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8C BINDING SITE, designated SEQ ID:18026, to the nucleotide sequence of

VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37998] Another function of VGAM1032 is therefore inhibition of Sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase) (SIAT8C, Accession NM_015879). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8C. Ubiquitin Specific Protease 24 (USP24, Accession XM_165973) is another VGAM1032 host target gene. USP24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP24 BINDING SITE, designated SEQ ID:43816, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[37999] Another function of VGAM1032 is therefore inhibition of Ubiquitin Specific Protease 24 (USP24, Accession XM_165973). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP24. LOC115330

(Accession NM_138445) is another VGAM1032 host target gene. LOC115330 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115330 BINDING SITE, designated SEQ ID:28809, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38000] Another function of VGAM1032 is therefore inhibition of LOC115330 (Accession NM_138445). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115330. LOC149650 (Accession XM_086623) is another VGAM1032 host target gene. LOC149650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149650 BINDING SITE, designated SEQ ID:38792, to the nucleotide sequence of VGAM1032 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3743.

[38001] Another function of VGAM1032 is therefore inhibition of LOC149650 (Accession XM_086623). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149650. LOC158046 (Accession NM_145283) is another VGAM1032 host target gene. LOC158046 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158046 BINDING SITE, designated SEQ ID:29799, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38002] Another function of VGAM1032 is therefore inhibition of LOC158046 (Accession NM_145283). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158046. LOC220565 (Accession XM_165417) is another VGAM1032 host target gene. LOC220565 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220565, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220565 BINDING SITE, designated SEQ ID:43633, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38003] Another function of VGAM1032 is therefore inhibition of LOC220565 (Accession XM_165417). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220565. LOC222031 (Accession XM_168371) is another VGAM1032 host target gene. LOC222031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222031 BINDING SITE, designated SEQ ID:45132, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38004] Another function of VGAM1032 is therefore inhibition of LOC222031 (Accession XM_168371). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC222031. LOC222962 (Accession XM_167291) is another VGAM1032 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44627, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38005] Another function of VGAM1032 is therefore inhibition of LOC222962 (Accession XM_167291). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. LOC256867 (Accession XM_170694) is another VGAM1032 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45472, to

the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38006] Another function of VGAM1032 is therefore inhibition of LOC256867 (Accession XM_170694). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. LOC91923 (Accession XM_041526) is another VGAM1032 host target gene. LOC91923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91923 BINDING SITE, designated SEQ ID:33544, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38007] Another function of VGAM1032 is therefore inhibition of LOC91923 (Accession XM_041526). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91923. LOC92299 (Accession XM_044075) is another VGAM1032 host target gene. LOC92299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC92299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92299 BINDING SITE, designated SEQ ID:34129, to the nucleotide sequence of VGAM1032 RNA, herein designated VGAM RNA, also designated SEQ ID:3743.

[38008] Another function of VGAM1032 is therefore inhibition of LOC92299 (Accession XM_044075). Accordingly, utilities of VGAM1032 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92299. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1033 (VGAM1033) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38009] VGAM1033 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1033 was detected is described hereinabove with reference to Figs. 1-8.

[38010] VGAM1033 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38011] VGAM1033 gene encodes a VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1033 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1033 precursor RNA is designated SEQ ID:1019, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1019 is located at position 105205 relative to the genome of Cercopithecine Herpesvirus 7.

[38012] VGAM1033 precursor RNA folds onto itself, forming VGAM1033 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38013] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1033 folded precursor RNA into VGAM1033 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1033 RNA is designated SEQ ID:3744, and is provided hereinbelow with reference to the sequence listing part.

[38014] VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1033 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38015] VGAM1033 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1033 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1033 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38016] The complementary binding of VGAM1033 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1033 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1033

host target RNA into VGAM1033 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38017] It is appreciated that VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1033 host target genes. The mRNA of each one of this plurality of VGAM1033 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1033 RNA, herein designated VGAM RNA, and which when bound by VGAM1033 RNA causes inhibition of translation of respective one or more VGAM1033 host target proteins.

[38018] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1033 gene, herein designated VGAM GENE, on one or more VGAM1033 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38019] It is yet further appreciated that a function of VGAM1033 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1033 correlate with, and may be deduced from, the identity of the host target genes which VGAM1033 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38020] Nucleotide sequences of the VGAM1033 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1033 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1033 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1033 are further

described hereinbelow with reference to Table 1.

[38021] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1033 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1033 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38022] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1033 gene, herein designated VGAM is inhibition of expression of VGAM1033 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1033 correlate with, and may be deduced from, the identity of the target genes which VGAM1033 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38023] BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519) is a VGAM1033 host target gene. BRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of BRF1 BINDING SITE, designated SEQ ID:7256, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38024] A function of VGAM1033 is therefore inhibition of BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519), a gene which is a general activator of RNA polymerase III. Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRF1. The function of BRF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232.CD34 Antigen (CD34, Accession NM_001773) is another VGAM1033 host target gene. CD34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD34 BINDING SITE, designated SEQ ID:7533, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3744.

[38025] Another function of VGAM1033 is therefore inhibition of CD34 Antigen (CD34, Accession NM_001773), a gene which is a monomeric cell surface antigen that is selectively expressed on human hematopoietic progenitor cells. Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD34. The function of CD34 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491) is another VGAM1033 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:27844 and SEQ ID:14648 respectively, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38026] Another function of VGAM1033 is therefore inhibition of

GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53. Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_139202) is another VGAM1033 host target gene. MLC1 BINDING SITE1 and MLC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MLC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLC1 BINDING SITE1 and MLC1 BINDING SITE2, designated SEQ ID:29215 and SEQ ID:10311 respectively, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38027] Another function of VGAM1033 is therefore inhibition of Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_139202). Accordingly, utili-

ties of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLC1. DKFZP434B195 (Accession NM_031284) is another VGAM1033 host target gene. DKFZP434B195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434B195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B195 BINDING SITE, designated SEQ ID:25309, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38028] Another function of VGAM1033 is therefore inhibition of DKFZP434B195 (Accession NM_031284). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B195. FLJ20195 (Accession NM_017706) is another VGAM1033 host target gene. FLJ20195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ20195 BINDING SITE, designated SEQ ID:19281, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38029] Another function of VGAM1033 is therefore inhibition of FLJ20195 (Accession NM_017706). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20195. Interleukin 18 Binding Protein (IL18BP, Accession NM_005699) is another VGAM1033 host target gene. IL18BP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL18BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL18BP BINDING SITE, designated SEQ ID:12252, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38030] Another function of VGAM1033 is therefore inhibition of Interleukin 18 Binding Protein (IL18BP, Accession NM_005699). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with IL18BP. KIAA1196 (Accession XM_028968) is another VGAM1033 host target gene. KIAA1196 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1196 BINDING SITE, designated SEQ ID:30820, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38031] Another function of VGAM1033 is therefore inhibition of KIAA1196 (Accession XM_028968). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1196. RASD Family, Member 2 (RASD2, Accession NM_014310) is another VGAM1033 host target gene. RASD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RASD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASD2 BINDING SITE, designated SEQ

ID:15605, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38032] Another function of VGAM1033 is therefore inhibition of RASD Family, Member 2 (RASD2, Accession NM_014310). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASD2. SCAMP5 (Accession NM_138967) is another VGAM1033 host target gene. SCAMP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP5 BINDING SITE, designated SEQ ID:29072, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38033] Another function of VGAM1033 is therefore inhibition of SCAMP5 (Accession NM_138967). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP5. Sialyltransferase 8D (alpha-2,

8-polysialyltransferase) (SIAT8D, Accession NM_005668) is another VGAM1033 host target gene. SIAT8D BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT8D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT8D BINDING SITE, designated SEQ ID:12223, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38034] Another function of VGAM1033 is therefore inhibition of Sialyltransferase 8D (alpha-2, 8-polysialyltransferase) (SIAT8D, Accession NM_005668). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT8D. TRIP-Br2 (Accession NM_014755) is another VGAM1033 host target gene. TRIP-Br2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRIP-Br2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16492, to the nucleotide sequence of

VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38035] Another function of VGAM1033 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. LOC123242 (Accession XM_063548) is another VGAM1033 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37241, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38036] Another function of VGAM1033 is therefore inhibition of LOC123242 (Accession XM_063548). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123242. LOC124245 (Accession NM_144604) is another VGAM1033 host target gene. LOC124245 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC124245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124245 BINDING SITE, designated SEQ ID:29419, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38037] Another function of VGAM1033 is therefore inhibition of LOC124245 (Accession NM_144604). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124245. LOC129303 (Accession XM_059343) is another VGAM1033 host target gene. LOC129303 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129303 BINDING SITE, designated SEQ ID:36970, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38038] Another function of VGAM1033 is therefore inhibition of LOC129303 (Accession XM_059343). Accordingly, utilities

of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129303. LOC130497 (Accession XM_059439) is another VGAM1033 host target gene. LOC130497 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130497 BINDING SITE, designated SEQ ID:36993, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38039] Another function of VGAM1033 is therefore inhibition of LOC130497 (Accession XM_059439). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130497. LOC150319 (Accession XM_086816) is another VGAM1033 host target gene. LOC150319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150319 BINDING SITE, designated SEQ ID:38891, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38040] Another function of VGAM1033 is therefore inhibition of LOC150319 (Accession XM_086816). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150319. LOC222962 (Accession XM_167291) is another VGAM1033 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44628, to the nucleotide sequence of VGAM1033 RNA, herein designated VGAM RNA, also designated SEQ ID:3744.

[38041] Another function of VGAM1033 is therefore inhibition of LOC222962 (Accession XM_167291). Accordingly, utilities of VGAM1033 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1034 (VGAM1034) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38042] VGAM1034 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1034 was detected is described hereinabove with reference to Figs. 1–8.

[38043] VGAM1034 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38044] VGAM1034 gene encodes a VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1034 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1034 precursor RNA is designated SEQ ID:1020, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1020 is located at position 108515 relative to the

genome of Cercopithecine Herpesvirus 7.

[38045] VGAM1034 precursor RNA folds onto itself, forming VGAM1034 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38046] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1034 folded precursor RNA into VGAM1034 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1034 RNA is designated SEQ ID:3745, and is provided hereinbelow with reference to the sequence listing part.

[38047] VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1034 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[38048] VGAM1034 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1034 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1034 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38049] The complementary binding of VGAM1034 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1034 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1034 host target RNA into VGAM1034 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38050] It is appreciated that VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1034 host target genes. The mRNA of each one of this plurality of VGAM1034 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1034 RNA, herein designated VGAM RNA, and which when bound by VGAM1034 RNA causes inhibition of translation of respective one or more VGAM1034 host target proteins.

[38051] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1034 gene, herein designated VGAM GENE, on one or more VGAM1034 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38052] It is yet further appreciated that a function of VGAM1034 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of

VGAM1034 correlate with, and may be deduced from, the identity of the host target genes which VGAM1034 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38053] Nucleotide sequences of the VGAM1034 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1034 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1034 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1034 are further described hereinbelow with reference to Table 1.

[38054] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1034 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1034 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38055] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1034 gene, herein designated VGAM is inhibition of expression of VGAM1034 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1034 correlate with, and may be deduced

from, the identity of the target genes which VGAM1034 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38056] Protocadherin Alpha 1 (PCDHA1, Accession NM_031411) is a VGAM1034 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:25383 and SEQ ID:20864 respectively, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38057] A function of VGAM1034 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_031411). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_018901) is another VGAM1034 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in

untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:20874 and SEQ ID:20884 respectively, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38058] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_018901). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM1034 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20905, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38059] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM_018905) is another VGAM1034 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20915, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38060] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM_018905). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM1034 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20925, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38061] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM1034 host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20935, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38062] Another function of VGAM1034 is therefore inhibition of

Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM_018908) is another VGAM1034 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20945, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38063] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM_018908). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM_018909) is another VGAM1034 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, cor-

responding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:20955 and SEQ ID:25587 respectively, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38064] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 6 (PCDHA6, Accession NM_018909). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM_018911) is another VGAM1034 host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20975, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38065] Another function of VGAM1034 is therefore inhibition of

Protocadherin Alpha 8 (PCDHA8, Accession NM_018911). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM1034 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25600, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38066] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM1034 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated SEQ ID:20844, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38067] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899) is another VGAM1034 host target gene. PCDHAC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

PCDHAC2 BINDING SITE, designated SEQ ID:20854, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38068] Another function of VGAM1034 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899). Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM_144585) is another VGAM1034 host target gene. SLC22A12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC22A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC22A12 BINDING SITE, designated SEQ ID:29402, to the nucleotide sequence of VGAM1034 RNA, herein designated VGAM RNA, also designated SEQ ID:3745.

[38069] Another function of VGAM1034 is therefore inhibition of Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM_144585), a gene which is a urate -anion exchanger regulating blood

urate levels. Accordingly, utilities of VGAM1034 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC22A12. The function of SLC22A12 has been established by previous studies.

Enomoto et al. (2002) isolated a SLC22A12 cDNA from a human kidney cDNA library. The cDNA, which they called URAT1 for 'urate transporter-1,' corresponds to a gene of 2,642 basepairs encoding a protein of 555 amino acids, which they called URAT1 for 'urate transporter-1,' that is 42% identical to OAT4 (OMIM Ref. No. 607097). The hydropathy plot predicts 12 membrane-spanning domains in URAT1, which are similar to those in members of the OAT family. URAT1 has 3 consensus sequences for N-glycosylation and 2 cyclic AMP-dependent protein kinase phosphorylation sites. High stringency Northern analysis revealed predominant expression of URAT1 mRNA in the human adult and fetal kidney, and immunohistochemical analysis revealed that URAT1 protein is prominent in epithelial cells of the proximal tubule of the renal cortex. Under high magnification, the protein was found to be located in the luminal membrane of the epithelium of proximal tubules but not in that of distal tubules Enomoto et al. (2002) demonstrated that *Xenopus* oocytes injected

with URAT1 cRNA exhibited time-dependent transport activity of [14C]urate but not of various typical substrates of OATs or organic cation transporters. URAT1 was found to be a cotransporter with anions, in particular chloride, bromide, or iodine, but not fluoride. Enomoto et al. (2002) found that urate transport via URAT1 is inhibited selectively by organic anions such as lactate, nicotinate, acetoacetate, hydroxybutyrate, and succinate. Para-aminohippurate (PAH), the representative substrate of OATs, did not exert an inhibitory effect on urate uptake via URAT1, consistent with the observation that PAH has no effect on the fractional excretion of urate in humans. Benzbromarone, probenecid, phenylbutazone, sulfinpyrazone, nonsteroidal antiinflammatory drugs, and diuretics inhibited urate uptake. Trans-stimulation experiments indicated that the major counteranions that exchange for urate via URAT1 are organic anions rather than inorganic chloride. Patients with renal hypouricemia (OMIM Ref. No. 220150) have mutations in URAT1.

[38070] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38071] Enomoto, A.; Kimura, H.; Chairoungdua, A.; Shigeta, Y.;

Jutabha, P.; Cha, S. H.; Hosoyamada, M.; Takeda, M.; Sekine, T.; Igarashi, T.; Matsuo, H.; Kikuchi, Y.; Oda, T.; Ichida, K.; Hosoya, T.; Shimokata, K.; Niwa, T.; Kanai, Y.; Endou, H. : Molecular identification of a renal urate–anion exchanger that regulates blood urate levels. *Nature* 417: 447–452, 2002. ; and

[38072] Enomoto, A.; Kimura, H.; Chairoungdua, A.; Shigeta, Y.; Jutabha, P.; Cha, S. H.; Hosoyamada, M.; Takeda, M.; Sekine, T.; Igarashi, T.; Matsuo, H.; Kikuchi, Y.; Oda, T.; Ichida, K.; Hosoya.

[38073] Further studies establishing the function and utilities of SLC22A12 are found in John Hopkins OMIM database record ID 607096, and in cited publications numbered 10108 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1035 (VGAM1035) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38074] VGAM1035 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1035 was detected is described hereinabove with reference to Figs. 1–8.

[38075] VGAM1035 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38076] VGAM1035 gene encodes a VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1035 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1035 precursor RNA is designated SEQ ID:1021, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1021 is located at position 105937 relative to the genome of Cercopithecine Herpesvirus 7.

[38077] VGAM1035 precursor RNA folds onto itself, forming VGAM1035 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38078] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1035 folded precursor RNA into VGAM1035 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1035 RNA is designated SEQ ID:3746, and is provided hereinbelow with reference to the sequence listing part.

[38079] VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1035 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38080] VGAM1035 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1035 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1035 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38081] The complementary binding of VGAM1035 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1035 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1035 host target RNA into VGAM1035 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38082] It is appreciated that VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1035 host target genes. The mRNA of each one of this plurality of VGAM1035 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1035 RNA, herein designated VGAM RNA, and which when bound by VGAM1035 RNA causes inhibition of translation of respective one or more VGAM1035 host target proteins.

[38083] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1035 gene, herein designated VGAM GENE, on one or more VGAM1035 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38084] It is yet further appreciated that a function of VGAM1035 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1035 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1035 correlate with, and may be deduced from, the identity of the host target genes which VGAM1035 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38085] Nucleotide sequences of the VGAM1035 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1035 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1035 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1035 are further described hereinbelow with reference to Table 1.

[38086] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1035 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1035 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38087] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1035 gene, herein designated VGAM is inhibition of expression of VGAM1035 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1035 correlate with, and may be deduced from, the identity of the target genes which VGAM1035 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38088] CRACC (Accession NM_021181) is a VGAM1035 host target gene. CRACC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRACC, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRACC BINDING SITE, designated SEQ ID:22152, to the nucleotide sequence of VGAM1035 RNA, herein designated VGAM RNA, also designated SEQ ID:3746.

[38089] A function of VGAM1035 is therefore inhibition of CRACC (Accession NM_021181), a gene which may participate in adhesion reactions between t lymphocytes and accessory cells. Accordingly, utilities of VGAM1035 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRACC. The function of CRACC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM26.LOC112885 (Accession NM_138415) is another VGAM1035 host target gene. LOC112885 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112885, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112885 BINDING SITE, designated SEQ ID:28785, to

the nucleotide sequence of VGAM1035 RNA, herein designated VGAM RNA, also designated SEQ ID:3746.

[38090] Another function of VGAM1035 is therefore inhibition of LOC112885 (Accession NM_138415). Accordingly, utilities of VGAM1035 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112885. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1036 (VGAM1036) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38091] VGAM1036 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1036 was detected is described hereinabove with reference to Figs. 1–8.

[38092] VGAM1036 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38093] VGAM1036 gene encodes a VGAM1036 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1036 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1036 precursor RNA is designated SEQ ID:1022, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1022 is located at position 108759 relative to the genome of Cercopithecine Herpesvirus 7.

[38094] VGAM1036 precursor RNA folds onto itself, forming VGAM1036 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38095] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1036 folded precursor RNA into VGAM1036 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1036 RNA is designated SEQ ID:3747, and is provided hereinbelow with reference to the sequence listing part.

[38096] VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1036 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38097] VGAM1036 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1036 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1036 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38098] The complementary binding of VGAM1036 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1036 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1036 host target RNA into VGAM1036 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38099] It is appreciated that VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1036 host target genes. The mRNA of each one of this plurality of VGAM1036 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1036 RNA, herein designated VGAM RNA, and which when bound by VGAM1036 RNA causes inhibition of translation of respective one or more VGAM1036 host target proteins.

[38100] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1036 gene, herein designated VGAM GENE, on one or more VGAM1036 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[38101] It is yet further appreciated that a function of VGAM1036 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1036 correlate with, and may be deduced from, the identity of the host target genes which VGAM1036 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38102] Nucleotide sequences of the VGAM1036 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1036 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1036 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1036 are further described hereinbelow with reference to Table 1.

[38103] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1036 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1036 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38104] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1036 gene, herein designated VGAM is inhibition of expression of VGAM1036 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1036 correlate with, and may be deduced from, the identity of the target genes which VGAM1036 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38105] Retinoic Acid Induced 14 (RAI14, Accession NM_015577) is a VGAM1036 host target gene. RAI14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI14 BINDING SITE, designated SEQ ID:17847, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38106] A function of VGAM1036 is therefore inhibition of Retinoic Acid Induced 14 (RAI14, Accession NM_015577), a gene

which is required for protein transport from the er to the golgi complex. Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI14. The function of RAI14 has been established by previous studies. Nagase et al. (2000) isolated a cDNA encoding RAI14, which they called KIAA1334, from a size-fractionated fetal brain cDNA library. Kutty et al. (2001) characterized the RAI14 gene, which they called NORPEG, from human retinal pigment epithelial cells (ARPE-19), in which its expression is induced by all-trans-retinoic acid. The predicted human and mouse proteins contain 980 and 979 amino acids, respectively, and share 84% sequence identity. Human RAI14 has a predicted molecular mass of 110 kD, a pI of 5.83, 6 potential N-glycosylation sites, several ankyrin repeats, and several coiled-coil helical domains. Northern blot analysis of human tissues detected expression of 2 transcripts of approximately 5 and 3 kb. Like the ARPE-19 cells, placenta showed an intense signal at 5 kb and a weak signal at 3 kb; the reverse was observed in testis, with an intense signal at 3 kb and a weak signal at 5 kb. RAI14 was also highly expressed in several human cancer cell lines. Expression studies showed that RAI14 localizes

to the cytoplasm. Confocal microscopic analysis in ARPE-19 cells showed threadlike projections in the cytoplasm reminiscent of the cytoskeleton. The expression of Rai14 was detected in mouse embryo at embryonic day 9.5 by in situ hybridization, and the expression appeared to be developmentally regulated. In adult mouse, the highest level of expression was detected in the seminiferous tubules of testis.

[38107] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38108] Kutty, R. K.; Kutty, G.; Samuel, W.; Duncan, T.; Bridges, C. C.; El-Sherbeeney, A.; Nagineni, C. N.; Smith, S. B.; Wiggert, B. : Molecular characterization and developmental expression of NORPEG, a novel gene induced by retinoic acid. J. Biol. Chem. 276: 2831-2840, 2001. ; and

[38109] Nagase, T.; Kikuno, R.; Ishikawa, K.; Hirose, M.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XVI. The complete sequences of 150 new cDNA clones from.

[38110] Further studies establishing the function and utilities of RAI14 are found in John Hopkins OMIM database record ID 606586, and in cited publications numbered 627 and

6371 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. UV Radiation Resistance Associated Gene (UVRAG, Accession NM_003369) is another VGAM1036 host target gene. UVRAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UVRAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UVRAG BINDING SITE, designated SEQ ID:9393, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38111] Another function of VGAM1036 is therefore inhibition of UV Radiation Resistance Associated Gene (UVRAG, Accession NM_003369). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UVRAG. Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926) is another VGAM1036 host target gene. ZFP36L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP36L1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP36L1 BINDING SITE, designated SEQ ID:11365, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38112] Another function of VGAM1036 is therefore inhibition of Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926), a gene which is a regulatory protein involved in regulating the response to growth factors. Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP36L1. The function of ZFP36L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM_027172) is another VGAM1036 host target gene. C1orf34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

C1orf34 BINDING SITE, designated SEQ ID:30439, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38113] Another function of VGAM1036 is therefore inhibition of Chromosome 1 Open Reading Frame 34 (C1orf34, Accession XM_027172). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf34. HYPH (Accession XM_170722) is another VGAM1036 host target gene. HYPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HYPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYPH BINDING SITE, designated SEQ ID:45484, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38114] Another function of VGAM1036 is therefore inhibition of HYPH (Accession XM_170722). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYPH. KIAA1719 (Accession XM_042936) is another VGAM1036 host target gene. KIAA1719 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33828, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38115] Another function of VGAM1036 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM_003958) is another VGAM1036 host target gene. RNF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF8 BINDING SITE, designated SEQ ID:10100, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38116] Another function of VGAM1036 is therefore inhibition of

Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM_003958). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF8. Zinc Metalloproteinase (STE24 homolog, yeast) (ZMPSTE24, Accession NM_005857) is another VGAM1036 host target gene. ZMPSTE24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZMPSTE24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZMPSTE24 BINDING SITE, designated SEQ ID:12462, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38117] Another function of VGAM1036 is therefore inhibition of Zinc Metalloproteinase (STE24 homolog, yeast) (ZMPSTE24, Accession NM_005857). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZMPSTE24. LOC200301 (Accession XM_114197) is another VGAM1036 host target gene. LOC200301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC200301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200301 BINDING SITE, designated SEQ ID:42781, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38118] Another function of VGAM1036 is therefore inhibition of LOC200301 (Accession XM_114197). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200301. LOC203286 (Accession XM_117526) is another VGAM1036 host target gene. LOC203286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43494, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38119] Another function of VGAM1036 is therefore inhibition of LOC203286 (Accession XM_117526). Accordingly, utilities

of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. LOC257479 (Accession XM_171548) is another VGAM1036 host target gene. LOC257479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257479 BINDING SITE, designated SEQ ID:46049, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38120] Another function of VGAM1036 is therefore inhibition of LOC257479 (Accession XM_171548). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257479. LOC51696 (Accession NM_016217) is another VGAM1036 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC51696 BINDING SITE, designated SEQ ID:18312, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38121] Another function of VGAM1036 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. LOC91907 (Accession XM_041430) is another VGAM1036 host target gene. LOC91907 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91907, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91907 BINDING SITE, designated SEQ ID:33521, to the nucleotide sequence of VGAM1036 RNA, herein designated VGAM RNA, also designated SEQ ID:3747.

[38122] Another function of VGAM1036 is therefore inhibition of LOC91907 (Accession XM_041430). Accordingly, utilities of VGAM1036 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91907. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1037 (VGAM1037) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38123] VGAM1037 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1037 was detected is described hereinabove with reference to Figs. 1–8.

[38124] VGAM1037 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38125] VGAM1037 gene encodes a VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1037 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1037 precursor RNA is designated SEQ ID:1023, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1023 is located at position 96311 relative to the

genome of Molluscum Contagiosum Virus.

- [38126] VGAM1037 precursor RNA folds onto itself, forming VGAM1037 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38127] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1037 folded precursor RNA into VGAM1037 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1037 RNA is designated SEQ ID:3748, and is provided hereinbelow with reference to the sequence listing part.
- [38128] VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1037 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[38129] VGAM1037 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1037 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1037 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38130] The complementary binding of VGAM1037 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1037 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1037 host target RNA into VGAM1037 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38131] It is appreciated that VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1037 host target genes. The mRNA of each one of this plurality of VGAM1037 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1037 RNA, herein designated VGAM RNA, and which when bound by VGAM1037 RNA causes inhibition of translation of respective one or more VGAM1037 host target proteins.

[38132] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1037 gene, herein designated VGAM GENE, on one or more VGAM1037 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38133] It is yet further appreciated that a function of VGAM1037 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1037 include diagnosis, prevention and treatment of viral infection by Molluscum Contagiosum Virus. Specific functions, and accordingly utilities, of

VGAM1037 correlate with, and may be deduced from, the identity of the host target genes which VGAM1037 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38134] Nucleotide sequences of the VGAM1037 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1037 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1037 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1037 are further described hereinbelow with reference to Table 1.

[38135] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1037 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1037 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38136] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1037 gene, herein designated VGAM is inhibition of expression of VGAM1037 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1037 correlate with, and may be deduced

from, the identity of the target genes which VGAM1037 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38137] Collagen, Type XI, Alpha 2 (COL11A2, Accession NM_080680) is a VGAM1037 host target gene. COL11A2 BINDING SITE1 and COL11A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL11A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL11A2 BINDING SITE1 and COL11A2 BINDING SITE2, designated SEQ ID:27973 and SEQ ID:27978 respectively, to the nucleotide sequence of VGAM1037 RNA, herein designated VGAM RNA, also designated SEQ ID:3748.

[38138] A function of VGAM1037 is therefore inhibition of Collagen, Type XI, Alpha 2 (COL11A2, Accession NM_080680). Accordingly, utilities of VGAM1037 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL11A2. KIAA1388 (Accession XM_168030) is another VGAM1037 host target gene. KIAA1388 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

KIAA1388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1388 BINDING SITE, designated SEQ ID:44948, to the nucleotide sequence of VGAM1037 RNA, herein designated VGAM RNA, also designated SEQ ID:3748.

[38139] Another function of VGAM1037 is therefore inhibition of KIAA1388 (Accession XM_168030). Accordingly, utilities of VGAM1037 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1388. LOC147299 (Accession XM_085763) is another VGAM1037 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38330, to the nucleotide sequence of VGAM1037 RNA, herein designated VGAM RNA, also designated SEQ ID:3748.

[38140] Another function of VGAM1037 is therefore inhibition of LOC147299 (Accession XM_085763). Accordingly, utilities

of VGAM1037 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1038 (VGAM1038) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38141] VGAM1038 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1038 was detected is described hereinabove with reference to Figs. 1-8.

[38142] VGAM1038 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38143] VGAM1038 gene encodes a VGAM1038 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1038 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1038 precursor RNA is designated SEQ ID:1024, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1024 is located at position 96469 relative to the genome of Molluscum Contagiosum Virus.

- [38144] VGAM1038 precursor RNA folds onto itself, forming VGAM1038 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38145] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1038 folded precursor RNA into VGAM1038 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1038 RNA is designated SEQ ID:3749, and

is provided hereinbelow with reference to the sequence listing part.

[38146] VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1038 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38147] VGAM1038 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1038 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1038 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38148] The complementary binding of VGAM1038 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1038 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1038 host target RNA into VGAM1038 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38149] It is appreciated that VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1038 host target genes. The mRNA of each one of this plurality of VGAM1038 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1038 RNA, herein designated VGAM RNA, and which when bound by VGAM1038 RNA causes inhibition of translation of respective one or more VGAM1038 host target proteins.

[38150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1038 gene, herein designated VGAM GENE, on one or more VGAM1038 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38151] It is yet further appreciated that a function of VGAM1038 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1038 correlate with, and may be deduced from, the identity of the host target genes which VGAM1038 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38152] Nucleotide sequences of the VGAM1038 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1038 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1038 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1038 are further described hereinbelow with reference to Table 1.

[38153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1038 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1038 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38154] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1038 gene, herein designated VGAM is inhibition of expression of VGAM1038 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1038 correlate with, and may be deduced from, the identity of the target genes which VGAM1038 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38155] Chaperone, ABC1 Activity of Bc1 Complex Like (*S. pombe*) (CABC1, Accession NM_020247) is a VGAM1038 host target gene. CABC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CABC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CABC1 BINDING SITE, designated SEQ ID:21540, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38156] A function of VGAM1038 is therefore inhibition of Chaperone, ABC1 Activity of Bc1 Complex Like (*S. pombe*) (CABC1, Accession NM_020247). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CABC1.

Neuron Navigator 2 (NAV2, Accession XM_012028) is another VGAM1038 host target gene. NAV2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAV2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAV2 BINDING SITE, designated SEQ ID:30203, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38157] Another function of VGAM1038 is therefore inhibition of Neuron Navigator 2 (NAV2, Accession XM_012028), a gene which plays an important role in neuronal development, including neurite outgrowth. Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAV2. The function of NAV2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481. Promyelocytic Leukemia (PML, Accession NM_033245) is another VGAM1038 host target gene. PML BINDING SITE1 and PML BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of

mRNA encoded by PML, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE1 and PML BINDING SITE2, designated SEQ ID:27084 and SEQ ID:27080 respectively, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38158] Another function of VGAM1038 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM_033245). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. DKFZP547L112 (Accession XM_039353) is another VGAM1038 host target gene. DKFZP547L112 BINDING SITE1 and DKFZP547L112 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP547L112, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP547L112 BINDING SITE1 and DKFZP547L112 BINDING SITE2, designated SEQ ID:33059 and SEQ ID:33055 respectively, to the nucleotide sequence of VGAM1038

RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38159] Another function of VGAM1038 is therefore inhibition of DKFZP547L112 (Accession XM_039353). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP547L112. KIAA1691 (Accession XM_166523) is another VGAM1038 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44460, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38160] Another function of VGAM1038 is therefore inhibition of KIAA1691 (Accession XM_166523). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. KIAA1856 (Accession XM_166549) is another VGAM1038 host target gene. KIAA1856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1856 BINDING SITE, designated SEQ ID:44521, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38161] Another function of VGAM1038 is therefore inhibition of KIAA1856 (Accession XM_166549). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1856. PRO0386 (Accession NM_018562) is another VGAM1038 host target gene. PRO0386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0386 BINDING SITE, designated SEQ ID:20647, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38162] Another function of VGAM1038 is therefore inhibition of PRO0386 (Accession NM_018562). Accordingly, utilities of

VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0386. RAP140 (Accession NM_015224) is another VGAM1038 host target gene. RAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP140 BINDING SITE, designated SEQ ID:17556, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38163] Another function of VGAM1038 is therefore inhibition of RAP140 (Accession NM_015224). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP140. Serologically Defined Colon Cancer Antigen 3 (SDCCAG3, Accession NM_006643) is another VGAM1038 host target gene. SDCCAG3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SDCCAG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SDCCAG3 BINDING SITE, designated SEQ ID:13434, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38164] Another function of VGAM1038 is therefore inhibition of Serologically Defined Colon Cancer Antigen 3 (SDCCAG3, Accession NM_006643). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDCCAG3. LOC122769 (Accession XM_058657) is another VGAM1038 host target gene. LOC122769 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122769 BINDING SITE, designated SEQ ID:36694, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38165] Another function of VGAM1038 is therefore inhibition of LOC122769 (Accession XM_058657). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC122769. LOC256901 (Accession XM_172952) is another VGAM1038 host target gene. LOC256901 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256901 BINDING SITE, designated SEQ ID:46206, to the nucleotide sequence of VGAM1038 RNA, herein designated VGAM RNA, also designated SEQ ID:3749.

[38166] Another function of VGAM1038 is therefore inhibition of LOC256901 (Accession XM_172952). Accordingly, utilities of VGAM1038 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256901. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1039 (VGAM1039) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38167] VGAM1039 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1039 was detected is described hereinabove with reference to Figs. 1–8.

[38168] VGAM1039 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mollusum Contagiosum Virus. VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38169] VGAM1039 gene encodes a VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1039 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1039 precursor RNA is designated SEQ ID:1025, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1025 is located at position 95607 relative to the genome of Mollusum Contagiosum Virus.

[38170] VGAM1039 precursor RNA folds onto itself, forming VGAM1039 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38171] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1039 folded precursor RNA into VGAM1039 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1039 RNA is designated SEQ ID:3750, and is provided hereinbelow with reference to the sequence listing part.

[38172] VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1039 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38173] VGAM1039 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1039 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1039 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38174] The complementary binding of VGAM1039 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1039 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1039 host target RNA into VGAM1039 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38175] It is appreciated that VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1039 host target genes. The mRNA of each one of this plurality of VGAM1039 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1039 RNA, herein designated VGAM RNA, and which when bound by VGAM1039 RNA causes inhibition of translation of respective one or more VGAM1039 host target proteins.

[38176] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1039 gene, herein designated VGAM GENE, on one or more VGAM1039 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38177] It is yet further appreciated that a function of VGAM1039 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of viral infection by Molluscum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1039 correlate with, and may be deduced from, the identity of the host target genes which VGAM1039 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38178] Nucleotide sequences of the VGAM1039 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1039 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1039 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1039 are further described hereinbelow with reference to Table 1.

[38179] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1039 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1039 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38180] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1039 gene, herein designated VGAM is inhibition of expression of VGAM1039 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1039 correlate with, and may be deduced from, the identity of the target genes which VGAM1039 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38181] A Disintegrin and Metalloproteinase Domain 12 (meltrin alpha) (ADAM12, Accession NM_003474) is a VGAM1039 host target gene. ADAM12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by ADAM12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM12 BINDING SITE, designated SEQ ID:9544, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38182] A function of VGAM1039 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 12 (meltrin alpha) (ADAM12, Accession NM_003474), a gene which involved in skeletal muscle regeneration, specifically at the onset of cell fusion. Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM12. The function of ADAM12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675.Cyclin-dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM_058197) is another VGAM1039 host target gene. CDKN2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN2A, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2A BINDING SITE, designated SEQ ID:27758, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38183] Another function of VGAM1039 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A, Accession NM_058197). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2A. Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487) is another VGAM1039 host target gene. CDKN2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2B BINDING SITE, designated SEQ ID:27808, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38184] Another function of VGAM1039 is therefore inhibition of

Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2B. Cerebellin 1 Precursor (CBLN1, Accession NM_004352) is another VGAM1039 host target gene. CBLN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBLN1 BINDING SITE, designated SEQ ID:10558, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38185] Another function of VGAM1039 is therefore inhibition of Cerebellin 1 Precursor (CBLN1, Accession NM_004352). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBLN1. KIAA1904 (Accession XM_056282) is another VGAM1039 host target gene. KIAA1904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

KIAA1904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE, designated SEQ ID:36380, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38186] Another function of VGAM1039 is therefore inhibition of KIAA1904 (Accession XM_056282). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. Retinoic Acid Induced 1 (RAI1, Accession XM_016259) is another VGAM1039 host target gene. RAI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI1 BINDING SITE, designated SEQ ID:30254, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38187] Another function of VGAM1039 is therefore inhibition of Retinoic Acid Induced 1 (RAI1, Accession XM_016259).

Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI1. RINZF (Accession NM_023929) is another VGAM1039 host target gene. RINZF BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RINZF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RINZF BINDING SITE, designated SEQ ID:23412, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38188] Another function of VGAM1039 is therefore inhibition of RINZF (Accession NM_023929). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RINZF. SH3 and Multiple Ankyrin Repeat Domains 3 (SHANK3, Accession XM_037493) is another VGAM1039 host target gene. SHANK3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SHANK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SHANK3 BINDING SITE, designated SEQ ID:32635, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38189] Another function of VGAM1039 is therefore inhibition of SH3 and Multiple Ankyrin Repeat Domains 3 (SHANK3, Accession XM_037493). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHANK3.

LOC201292 (Accession XM_113949) is another VGAM1039 host target gene. LOC201292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201292 BINDING SITE, designated SEQ ID:42564, to the nucleotide sequence of VGAM1039 RNA, herein designated VGAM RNA, also designated SEQ ID:3750.

[38190] Another function of VGAM1039 is therefore inhibition of LOC201292 (Accession XM_113949). Accordingly, utilities of VGAM1039 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC201292. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1040 (VGAM1040) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38191] VGAM1040 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1040 was detected is described hereinabove with reference to Figs. 1–8.

[38192] VGAM1040 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Molluscum Contagiosum Virus. VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38193] VGAM1040 gene encodes a VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1040 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1040 precursor RNA is designated SEQ ID:1026, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1026 is located at position 92882 relative to the genome of Molluscum Contagiosum Virus.

- [38194] VGAM1040 precursor RNA folds onto itself, forming VGAM1040 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38195] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1040 folded precursor RNA into VGAM1040 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1040 RNA is designated SEQ ID:3751, and is provided hereinbelow with reference to the sequence listing part.

[38196] VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1040 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38197] VGAM1040 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1040 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1040 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38198] The complementary binding of VGAM1040 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1040 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1040 host target RNA into VGAM1040 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38199] It is appreciated that VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1040 host target genes. The mRNA of each one of this plurality of VGAM1040 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1040 RNA, herein designated VGAM RNA, and which when bound by VGAM1040 RNA causes

inhibition of translation of respective one or more VGAM1040 host target proteins.

[38200] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1040 gene, herein designated VGAM GENE, on one or more VGAM1040 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38201] It is yet further appreciated that a function of VGAM1040 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1040 include diagnosis, prevention and

treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGAM1040 correlate with, and may be deduced from, the identity of the host target genes which VGAM1040 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38202] Nucleotide sequences of the VGAM1040 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1040 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1040 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1040 are further described hereinbelow with reference to Table 1.

[38203] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1040 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1040 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38204] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1040 gene, herein designated VGAM is inhibition of expression of VGAM1040 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1040 correlate with, and may be deduced from, the identity of the target genes which VGAM1040 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38205] Sodium Channel, Nonvoltage-gated 1 Alpha (SCNN1A, Accession NM_001038) is a VGAM1040 host target gene. SCNN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCNN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCNN1A BINDING SITE, designated SEQ ID:6702, to the nucleotide sequence of VGAM1040 RNA, herein designated VGAM RNA, also designated SEQ ID:3751.

[38206] A function of VGAM1040 is therefore inhibition of Sodium Channel, Nonvoltage-gated 1 Alpha (SCNN1A, Accession NM_001038). Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCNN1A. Degenerative Spermatocyte Homolog, Lipid Desaturase (Drosophila) (DEGS, Accession NM_003676) is another VGAM1040 host

target gene. DEGS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DEGS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEGS BINDING SITE, designated SEQ ID:9769, to the nucleotide sequence of VGAM1040 RNA, herein designated VGAM RNA, also designated SEQ ID:3751.

[38207] Another function of VGAM1040 is therefore inhibition of Degenerative Spermatocyte Homolog, Lipid Desaturase (Drosophila) (DEGS, Accession NM_003676). Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEGS. KIAA0040 (Accession NM_014656) is another VGAM1040 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16099, to the nucleotide sequence of VGAM1040 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3751.

[38208] Another function of VGAM1040 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. TNF Receptor-associated Factor 4 (TRAF4, Accession XM_031427) is another VGAM1040 host target gene. TRAF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF4 BINDING SITE, designated SEQ ID:31377, to the nucleotide sequence of VGAM1040 RNA, herein designated VGAM RNA, also designated SEQ ID:3751.

[38209] Another function of VGAM1040 is therefore inhibition of TNF Receptor-associated Factor 4 (TRAF4, Accession XM_031427). Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF4. LOC153196 (Accession XM_098323) is another VGAM1040 host target gene. LOC153196 BINDING SITE is HOST TARGET binding

site found in the 5' untranslated region of mRNA encoded by LOC153196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153196 BINDING SITE, designated SEQ ID:41585, to the nucleotide sequence of VGAM1040 RNA, herein designated VGAM RNA, also designated SEQ ID:3751.

[38210] Another function of VGAM1040 is therefore inhibition of LOC153196 (Accession XM_098323). Accordingly, utilities of VGAM1040 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153196. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1041 (VGAM1041) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38211] VGAM1041 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1041 was detected is described hereinabove with reference to Figs. 1-8.

[38212] VGAM1041 gene, herein designated VGAM GENE, is a viral gene contained in the genome of White Clover Mosaic Virus. VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38213] VGAM1041 gene encodes a VGAM1041 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1041 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1041 precursor RNA is designated SEQ ID:1027, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1027 is located at position 1636 relative to the genome of White Clover Mosaic Virus.

[38214] VGAM1041 precursor RNA folds onto itself, forming VGAM1041 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[38215] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1041 folded precursor RNA into VGAM1041 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1041 RNA is designated SEQ ID:3752, and is provided hereinbelow with reference to the sequence listing part.

[38216] VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1041 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38217] VGAM1041 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1041 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1041 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1041 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38218] The complementary binding of VGAM1041 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1041 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1041 host target RNA into VGAM1041 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38219] It is appreciated that VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1041 host target genes. The mRNA of each one of this plurality of VGAM1041 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1041 RNA, herein designated VGAM RNA, and which when bound by VGAM1041 RNA causes inhibition of translation of respective one or more VGAM1041 host target proteins.

[38220] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1041 gene, herein designated VGAM GENE, on one or more VGAM1041 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38221] It is yet further appreciated that a function of VGAM1041 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of viral infection by White Clover Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1041 correlate with, and may be deduced from, the identity of the host target genes which VGAM1041 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38222] Nucleotide sequences of the VGAM1041 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1041 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1041 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1041 are further described hereinbelow with reference to Table 1.

[38223] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1041 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1041 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38224] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1041 gene, herein designated VGAM is inhibition of expression of VGAM1041 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1041 correlate with, and may be deduced from, the identity of the target genes which VGAM1041 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38225] Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943) is a VGAM1041 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38410, to the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38226] A function of VGAM1041 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.BA108L7.2 (Accession NM_030971) is another VGAM1041 host target gene. BA108L7.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BA108L7.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BA108L7.2 BINDING SITE, designated SEQ ID:25236, to the nucleotide sequence of VGAM1041 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3752.

[38227] Another function of VGAM1041 is therefore inhibition of BA108L7.2 (Accession NM_030971). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BA108L7.2. CDT1 (Accession XM_085327) is another VGAM1041 host target gene. CDT1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CDT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDT1 BINDING SITE, designated SEQ ID:38068, to the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38228] Another function of VGAM1041 is therefore inhibition of CDT1 (Accession XM_085327). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDT1. KIAA0992 (Accession NM_016081) is another VGAM1041 host target gene. KIAA0992 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0992, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0992 BINDING SITE, designated SEQ ID:18155, to the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38229] Another function of VGAM1041 is therefore inhibition of KIAA0992 (Accession NM_016081). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0992. KIAA1181 (Accession XM_043340) is another VGAM1041 host target gene. KIAA1181 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1181 BINDING SITE, designated SEQ ID:33922, to the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38230] Another function of VGAM1041 is therefore inhibition of KIAA1181 (Accession XM_043340). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1181. MIG (Accession NM_002416) is another VGAM1041 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, designated SEQ ID:8242, to the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38231] Another function of VGAM1041 is therefore inhibition of MIG (Accession NM_002416). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. LOC196485 (Accession XM_113731) is another VGAM1041 host target gene. LOC196485 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196485 BINDING SITE, designated SEQ ID:42380, to

the nucleotide sequence of VGAM1041 RNA, herein designated VGAM RNA, also designated SEQ ID:3752.

[38232] Another function of VGAM1041 is therefore inhibition of LOC196485 (Accession XM_113731). Accordingly, utilities of VGAM1041 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196485. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1042 (VGAM1042) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38233] VGAM1042 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1042 was detected is described hereinabove with reference to Figs. 1–8.

[38234] VGAM1042 gene, herein designated VGAM GENE, is a viral gene contained in the genome of White Clover Mosaic Virus. VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38235] VGAM1042 gene encodes a VGAM1042 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1042 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1042 precursor RNA is designated SEQ ID:1028, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1028 is located at position 3519 relative to the genome of White Clover Mosaic Virus.

[38236] VGAM1042 precursor RNA folds onto itself, forming VGAM1042 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38237] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1042 folded precursor RNA into VGAM1042 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1042 RNA is designated SEQ ID:3753, and is provided hereinbelow with reference to the sequence listing part.

[38238] VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1042 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38239] VGAM1042 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1042 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1042 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38240] The complementary binding of VGAM1042 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1042 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1042 host target RNA into VGAM1042 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38241] It is appreciated that VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1042 host target genes. The mRNA of each one of this plurality of VGAM1042 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1042 RNA, herein designated VGAM RNA, and which when bound by VGAM1042 RNA causes inhibition of translation of respective one or more VGAM1042 host target proteins.

[38242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1042 gene, herein designated VGAM GENE, on one or more VGAM1042 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[38243] It is yet further appreciated that a function of VGAM1042 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of viral infection by White Clover Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1042 correlate with, and may be deduced from, the identity of the host target genes which VGAM1042 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38244] Nucleotide sequences of the VGAM1042 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1042 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1042 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1042 are further described hereinbelow with reference to Table 1.

[38245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1042 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1042 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38246] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1042 gene, herein designated VGAM is inhibition of expression of VGAM1042 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1042 correlate with, and may be deduced from, the identity of the target genes which VGAM1042 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38247] Endothelin 2 (EDN2, Accession NM_001956) is a VGAM1042 host target gene. EDN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDN2 BINDING SITE, designated SEQ ID:7681, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38248] A function of VGAM1042 is therefore inhibition of Endothelin 2 (EDN2, Accession NM_001956), a gene which is

a precursor of the hormone endothelin 2 which is an endothelium-derived vasoconstrictor peptide. Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDN2. The function of EDN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1015. Centaurin, Gamma 2 (CENTG2, Accession NM_014914) is another VGAM1042 host target gene. CENTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG2 BINDING SITE, designated SEQ ID:17156, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38249] Another function of VGAM1042 is therefore inhibition of Centaurin, Gamma 2 (CENTG2, Accession NM_014914). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG2. Carbohydrate

(N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769) is another VGAM1042 host target gene. CHST4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST4 BINDING SITE, designated SEQ ID:12336, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38250] Another function of VGAM1042 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST4. KIAA1889 (Accession XM_056298) is another VGAM1042 host target gene. KIAA1889 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1889, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1889 BINDING SITE,

designated SEQ ID:36386, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38251] Another function of VGAM1042 is therefore inhibition of KIAA1889 (Accession XM_056298). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1889. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942) is another VGAM1042 host target gene. RPS6KA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA4 BINDING SITE, designated SEQ ID:10053, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38252] Another function of VGAM1042 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

RPS6KA4. LOC151719 (Accession XM_087280) is another VGAM1042 host target gene. LOC151719 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151719 BINDING SITE, designated SEQ ID:39162, to the nucleotide sequence of VGAM1042 RNA, herein designated VGAM RNA, also designated SEQ ID:3753.

[38253] Another function of VGAM1042 is therefore inhibition of LOC151719 (Accession XM_087280). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151719. LOC255040 (Accession XM_172837) is another VGAM1042 host target gene. LOC255040 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255040 BINDING SITE, designated SEQ ID:46110, to the nucleotide sequence of VGAM1042 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3753.

[38254] Another function of VGAM1042 is therefore inhibition of LOC255040 (Accession XM_172837). Accordingly, utilities of VGAM1042 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255040. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1043 (VGAM1043) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38255] VGAM1043 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1043 was detected is described hereinabove with reference to Figs. 1–8.

[38256] VGAM1043 gene, herein designated VGAM GENE, is a viral gene contained in the genome of White Clover Mosaic Virus. VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38257] VGAM1043 gene encodes a VGAM1043 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1043 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1043 precursor RNA is designated SEQ ID:1029, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1029 is located at position 5056 relative to the genome of White Clover Mosaic Virus.

[38258] VGAM1043 precursor RNA folds onto itself, forming VGAM1043 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38259] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1043 folded precursor RNA into VGAM1043 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1043 RNA is designated SEQ ID:3754, and is provided hereinbelow with reference to the sequence listing part.

[38260] VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1043 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38261] VGAM1043 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1043 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1043 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38262] The complementary binding of VGAM1043 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1043 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1043 host target RNA into VGAM1043 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38263] It is appreciated that VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1043 host target genes. The mRNA of

each one of this plurality of VGAM1043 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1043 RNA, herein designated VGAM RNA, and which when bound by VGAM1043 RNA causes inhibition of translation of respective one or more VGAM1043 host target proteins.

[38264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1043 gene, herein designated VGAM GENE, on one or more VGAM1043 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[38265] It is yet further appreciated that a function of VGAM1043 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of viral infection by White Clover Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1043 correlate with, and may be deduced from, the identity of the host target genes which VGAM1043 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38266] Nucleotide sequences of the VGAM1043 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1043 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1043 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1043 are further described hereinbelow with reference to Table 1.

[38267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1043 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1043 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38268] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1043 gene, herein designated VGAM is inhibition of expression of VGAM1043 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1043 correlate with, and may be deduced from, the identity of the target genes which VGAM1043 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38269] Acyl-Coenzyme A Dehydrogenase, C-4 to C-12 Straight Chain (ACADM, Accession NM_000016) is a VGAM1043 host target gene. ACADM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACADM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADM BINDING SITE, designated SEQ ID:5452, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38270] A function of VGAM1043 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, C-4 to C-12 Straight Chain

(ACADM, Accession NM_000016). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADM. Adenylate Cyclase 9 (ADCY9, Accession NM_001116) is another VGAM1043 host target gene. ADCY9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY9 BINDING SITE, designated SEQ ID:6790, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38271] Another function of VGAM1043 is therefore inhibition of Adenylate Cyclase 9 (ADCY9, Accession NM_001116), a gene which . may be a physiologically relevant docking site for calcineurin (by similarity). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY9. The function of ADCY9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM477.ADP-ribosylation Factor 1 (ARF1, Accession XM_047545) is another VGAM1043 host target gene. ARF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF1 BINDING SITE, designated SEQ ID:34991, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38272] Another function of VGAM1043 is therefore inhibition of ADP-ribosylation Factor 1 (ARF1, Accession XM_047545). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF1. ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702) is another VGAM1043 host target gene. ATP1A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1A2 BINDING SITE, designated SEQ

ID:6368, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38273] Another function of VGAM1043 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1A2. Collagen, Type XV, Alpha 1 (COL15A1, Accession NM_001855) is another VGAM1043 host target gene. COL15A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL15A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL15A1 BINDING SITE, designated SEQ ID:7588, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38274] Another function of VGAM1043 is therefore inhibition of Collagen, Type XV, Alpha 1 (COL15A1, Accession NM_001855), a gene which may be involved in maintaining the structure of connective tissue. Accordingly, utili-

ties of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL15A1. The function of COL15A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM304. Casein Kinase 1, Gamma 3 (CSNK1G3, Accession NM_004384) is another VGAM1043 host target gene. CSNK1G3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSNK1G3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSNK1G3 BINDING SITE, designated SEQ ID:10609, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38275] Another function of VGAM1043 is therefore inhibition of Casein Kinase 1, Gamma 3 (CSNK1G3, Accession NM_004384). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSNK1G3. Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502) is another VGAM1043 host target gene.

CX3CR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CX3CR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CX3CR1 BINDING SITE, designated SEQ ID:34974, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38276] Another function of VGAM1043 is therefore inhibition of Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502), a gene which mediates both the adhesive and migratory functions of fractalkine. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CX3CR1. The function of CX3CR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25.DNA (cytosine-5-methyltransferase 2 (DNMT2, Accession NM_004412) is another VGAM1043 host target gene. DNMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DNMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT2 BINDING SITE, designated SEQ ID:10670, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38277] Another function of VGAM1043 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM_004412), a gene which may mark specific sequences in the genome . Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT2. The function of DNMT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM177.Desmocollin 3 (DSC3, Accession NM_024423) is another VGAM1043 host target gene. DSC3 BINDING SITE1 and DSC3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DSC3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of DSC3 BINDING SITE1 and DSC3 BINDING SITE2, designated SEQ ID:23664 and SEQ ID:7653 respectively, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38278] Another function of VGAM1043 is therefore inhibition of Desmocollin 3 (DSC3, Accession NM_024423), a gene which is a component of intercellular desmosome junctions. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSC3. The function of DSC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM230. Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052) is another VGAM1043 host target gene. DSCR3 BINDING SITE1 and DSCR3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DSCR3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR3 BINDING SITE1 and DSCR3 BINDING SITE2, designated SEQ ID:12686 and

SEQ ID:11722 respectively, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38279] Another function of VGAM1043 is therefore inhibition of Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR3. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7) (GALNT7, Accession NM_017423) is another VGAM1043 host target gene. GALNT7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT7 BINDING SITE, designated SEQ ID:18877, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38280] Another function of VGAM1043 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7) (GALNT7,

Accession NM_017423). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT7. Integral Membrane Protein 2B (ITM2B, Accession NM_021999) is another VGAM1043 host target gene. ITM2B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ITM2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITM2B BINDING SITE, designated SEQ ID:22540, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38281] Another function of VGAM1043 is therefore inhibition of Integral Membrane Protein 2B (ITM2B, Accession NM_021999), a gene which is a member of the type II integral membrane protein family. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITM2B. The function of ITM2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM458.Kinesin Family Member 3C (KIF3C, Accession NM_002254) is another VGAM1043 host target gene. KIF3C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIF3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3C BINDING SITE, designated SEQ ID:8058, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38282] Another function of VGAM1043 is therefore inhibition of Kinesin Family Member 3C (KIF3C, Accession NM_002254). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF3C. Latent Transforming Growth Factor Beta Binding Protein 1 (LTBP1, Accession NM_000627) is another VGAM1043 host target gene. LTBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LTBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTBP1 BINDING SITE, designated SEQ ID:6243,

to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38283] Another function of VGAM1043 is therefore inhibition of Latent Transforming Growth Factor Beta Binding Protein 1 (LTBP1, Accession NM_000627), a gene which is involved in assembly and secretion of latent TGF-beta. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTBP1. The function of LTBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM80. Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430) is another VGAM1043 host target gene. MN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MN1 BINDING SITE, designated SEQ ID:8275, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38284] Another function of VGAM1043 is therefore inhibition of

Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MN1. RNA Binding Motif Protein, X Chromosome (RBMX, Accession XM_042968) is another VGAM1043 host target gene. RBMX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RBMX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBMX BINDING SITE, designated SEQ ID:33857, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38285] Another function of VGAM1043 is therefore inhibition of RNA Binding Motif Protein, X Chromosome (RBMX, Accession XM_042968), a gene which binds rna as a component of the ribonucleosome. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBMX. The function of RBMX has been established by previous studies. The genes on the human Y chromosome fall into 2 classes with distinct evolutionary origins. Widely ex-

pressed, single-copy genes with X homologs that escape inactivation (X-Y shared genes) derive from the ancient proto X-Y chromosome pair. Testis-specific, multicopy genes with no X homologs originate from autosomes and have accumulated on a 'selfish Y' because of their male-specific function. Copies of genes in the RBMY gene family (see OMIM Ref. No. RBMY1A1, 400006) are candidate spermatogenesis genes because they are found in all 3 azoospermia factor (AZF) deletion intervals on the human Yq, which are associated with oligospermia or azoospermia (Vogt et al., 1997). An active X-borne homolog of the Y-borne RBMY gene was demonstrated in humans and marsupials by Delbridge et al. (1999) and in the mouse by Mazeyrat et al. (1999). Delbridge et al. (1999) stated that, like other gene pairs on the X and Y chromosomes (e.g., OMIM Ref. No. 400005), RBMX retained a widespread function and RBMY evolved a male-specific function in spermatogenesis. Thus, RBMY1A1, far from belonging to a 'second class' of testis-specific elements, is a diverged X-Y shared gene. Venables et al. (2000) used a yeast 2-hybrid system to show that the RBMY gene product hnRNP G and a novel testis-specific relative (termed hnRNP G-T) interact with Tra2-beta (OMIM Ref. No. 602719), an

activator of pre-mRNA splicing that is ubiquitous but highly expressed in testis. The RBMY gene product and Tra2-beta colocalized in 2 major domains in human spermatocyte nuclei. Incubation with the protein interaction domain of the RBMY gene product inhibited splicing in vitro of a specific pre-mRNA substrate containing an essential enhancer bound by Tra2-beta. The RNA-binding domain of RBM affected 5-prime splice site selection. The authors concluded that the hnRNP G family of proteins is involved in pre-mRNA splicing and hypothesized that RBM may be involved in Tra2-beta-dependent splicing in spermatocytes.

[38286] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38287] Delbridge, M. L.; Lingenfelter, P. A.; Disteche, C. M.; Marshall Graves, J. A. : The candidate spermatogenesis gene RBMY has a homologue on the human X chromosome. (Letter) Nature Genet. 22: 223-224, 1999. ; and

[38288] Venables, J. P.; Elliott, D. J.; Makarova, O. V.; Makarov, E. M.; Cooke, H. J.; Eperon, I. C. : RBMY, a probable human spermatogenesis factor, and other hnRNP G proteins interact with T.

[38289] Further studies establishing the function and utilities of RBMX are found in John Hopkins OMIM database record ID 300199, and in cited publications numbered 11402–11406 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Thy-1 Cell Surface Antigen (THY1, Accession NM_006288) is another VGAM1043 host target gene. THY1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by THY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THY1 BINDING SITE, designated SEQ ID:12977, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38290] Another function of VGAM1043 is therefore inhibition of Thy-1 Cell Surface Antigen (THY1, Accession NM_006288), a gene which plays a role in cell-cell or cell-ligand interactions during synaptogenesis. Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THY1. The function of THY1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM396. Activating Transcription Factor 3 (ATF3, Accession NM_004024) is another VGAM1043 host target gene. ATF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF3 BINDING SITE, designated SEQ ID:10245, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38291] Another function of VGAM1043 is therefore inhibition of Activating Transcription Factor 3 (ATF3, Accession NM_004024). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF3. ATPase, Class V, Type 10D (ATP10D, Accession XM_054907) is another VGAM1043 host target gene. ATP10D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP10D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ATP10D BINDING SITE, designated SEQ ID:36201, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38292] Another function of VGAM1043 is therefore inhibition of ATPase, Class V, Type 10D (ATP10D, Accession XM_054907). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10D. BA108L7.2 (Accession NM_030971) is another VGAM1043 host target gene. BA108L7.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BA108L7.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BA108L7.2 BINDING SITE, designated SEQ ID:25240, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38293] Another function of VGAM1043 is therefore inhibition of BA108L7.2 (Accession NM_030971). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

BA108L7.2. Chromosome 15 Open Reading Frame 5 (C15orf5, Accession NM_030944) is another VGAM1043 host target gene. C15orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C15orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C15orf5 BINDING SITE, designated SEQ ID:25214, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38294] Another function of VGAM1043 is therefore inhibition of Chromosome 15 Open Reading Frame 5 (C15orf5, Accession NM_030944). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C15orf5. Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424) is another VGAM1043 host target gene. CECR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CECR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of CECR1 BINDING SITE, designated SEQ ID:18883, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38295] Another function of VGAM1043 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR1. Centaurin, Alpha 2 (CENTA2, Accession NM_018404) is another VGAM1043 host target gene. CENTA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTA2 BINDING SITE, designated SEQ ID:20443, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38296] Another function of VGAM1043 is therefore inhibition of Centaurin, Alpha 2 (CENTA2, Accession NM_018404). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with CENTA2. CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM_003663) is another VGAM1043 host target gene. CGGBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CGGBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGGBP1 BINDING SITE, designated SEQ ID:9740, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38297] Another function of VGAM1043 is therefore inhibition of CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM_003663). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGGBP1. DKFZP434P211 (Accession NM_014549) is another VGAM1043 host target gene. DKFZP434P211 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434P211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P211 BINDING

SITE, designated SEQ ID:15868, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38298] Another function of VGAM1043 is therefore inhibition of DKFZP434P211 (Accession NM_014549). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P211. DKFZP547N043 (Accession NM_032018) is another VGAM1043 host target gene. DKFZP547N043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP547N043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP547N043 BINDING SITE, designated SEQ ID:25731, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38299] Another function of VGAM1043 is therefore inhibition of DKFZP547N043 (Accession NM_032018). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP547N043. DKFZP564M182 (Accession

XM_085525) is another VGAM1043 host target gene. DKFZP564M182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564M182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564M182 BINDING SITE, designated SEQ ID:38219, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38300] Another function of VGAM1043 is therefore inhibition of DKFZP564M182 (Accession XM_085525). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564M182. Cyclin D Binding Myb-like Transcription Factor 1 (DMTF1, Accession NM_021145) is another VGAM1043 host target gene. DMTF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMTF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMTF1 BINDING SITE, designated SEQ ID:22116, to the nucleotide se-

quence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38301] Another function of VGAM1043 is therefore inhibition of Cyclin D Binding Myb-like Transcription Factor 1 (DMTF1, Accession NM_021145). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMTF1. FBP17 (Accession XM_052666) is another VGAM1043 host target gene. FBP17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36049, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38302] Another function of VGAM1043 is therefore inhibition of FBP17 (Accession XM_052666). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ10392 (Accession NM_018084) is another VGAM1043 host target gene. FLJ10392 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by FLJ10392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10392 BINDING SITE, designated SEQ ID:19846, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38303] Another function of VGAM1043 is therefore inhibition of FLJ10392 (Accession NM_018084). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10392. FLJ10898 (Accession XM_002486) is another VGAM1043 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29893, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38304] Another function of VGAM1043 is therefore inhibition of

FLJ10898 (Accession XM_002486). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. FLJ11106 (Accession NM_018324) is another VGAM1043 host target gene. FLJ11106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11106 BINDING SITE, designated SEQ ID:20318, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38305] Another function of VGAM1043 is therefore inhibition of FLJ11106 (Accession NM_018324). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11106. FLJ14166 (Accession NM_024565) is another VGAM1043 host target gene. FLJ14166 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ14166 BINDING SITE, designated SEQ ID:23792, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38306] Another function of VGAM1043 is therefore inhibition of FLJ14166 (Accession NM_024565). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14166. FLJ20170 (Accession NM_017696) is another VGAM1043 host target gene. FLJ20170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20170 BINDING SITE, designated SEQ ID:19259, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38307] Another function of VGAM1043 is therefore inhibition of FLJ20170 (Accession NM_017696). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20170. FLJ22690 (Accession NM_024711) is another

VGAM1043 host target gene. FLJ22690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22690 BINDING SITE, designated SEQ ID:24038, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38308] Another function of VGAM1043 is therefore inhibition of FLJ22690 (Accession NM_024711). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22690. GLP (Accession NM_018652) is another VGAM1043 host target gene. GLP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLP BINDING SITE, designated SEQ ID:20723, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38309] Another function of VGAM1043 is therefore inhibition of GLP (Accession NM_018652). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLP. GOLGIN-67 (Accession XM_170772) is another VGAM1043 host target gene. GOLGIN-67 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGIN-67, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGIN-67 BINDING SITE, designated SEQ ID:45536, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38310] Another function of VGAM1043 is therefore inhibition of GOLGIN-67 (Accession XM_170772). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGIN-67. Interleukin 17D (IL17D, Accession NM_138284) is another VGAM1043 host target gene. IL17D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL17D, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL17D BINDING SITE, designated SEQ ID:28699, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38311] Another function of VGAM1043 is therefore inhibition of Interleukin 17D (IL17D, Accession NM_138284). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL17D. KIAA0152 (Accession NM_014730) is another VGAM1043 host target gene. KIAA0152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE, designated SEQ ID:16337, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38312] Another function of VGAM1043 is therefore inhibition of KIAA0152 (Accession NM_014730). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0152. KIAA0193 (Accession NM_014766) is another VGAM1043 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16538, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38313] Another function of VGAM1043 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. KIAA0254 (Accession NM_014758) is another VGAM1043 host target gene. KIAA0254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0254 BINDING SITE, designated SEQ ID:16503, to the nucleotide sequence of VGAM1043 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3754.

[38314] Another function of VGAM1043 is therefore inhibition of KIAA0254 (Accession NM_014758). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0254. KIAA0379 (Accession XM_042860) is another VGAM1043 host target gene. KIAA0379 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0379, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0379 BINDING SITE, designated SEQ ID:33812, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38315] Another function of VGAM1043 is therefore inhibition of KIAA0379 (Accession XM_042860). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0379. KIAA0603 (Accession NM_014832) is another VGAM1043 host target gene. KIAA0603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0603, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0603 BINDING SITE, designated SEQ ID:16829, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38316] Another function of VGAM1043 is therefore inhibition of KIAA0603 (Accession NM_014832). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0603. KIAA0620 (Accession XM_030707) is another VGAM1043 host target gene. KIAA0620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0620 BINDING SITE, designated SEQ ID:31122, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38317] Another function of VGAM1043 is therefore inhibition of KIAA0620 (Accession XM_030707). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0620. KIAA0855 (Accession NM_015003) is another VGAM1043 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17376, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38318] Another function of VGAM1043 is therefore inhibition of KIAA0855 (Accession NM_015003). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. KIAA0976 (Accession NM_014917) is another VGAM1043 host target gene. KIAA0976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0976 BINDING SITE, designated SEQ ID:17167, to the

nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38319] Another function of VGAM1043 is therefore inhibition of KIAA0976 (Accession NM_014917). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0976. KIAA1170 (Accession XM_045907) is another VGAM1043 host target gene. KIAA1170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1170 BINDING SITE, designated SEQ ID:34611, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38320] Another function of VGAM1043 is therefore inhibition of KIAA1170 (Accession XM_045907). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1170. KIAA1361 (Accession XM_030845) is another VGAM1043 host target gene. KIAA1361 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA1361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1361 BINDING SITE, designated SEQ ID:31165, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38321] Another function of VGAM1043 is therefore inhibition of KIAA1361 (Accession XM_030845). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1361. KIAA1789 (Accession XM_040486) is another VGAM1043 host target gene. KIAA1789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1789 BINDING SITE, designated SEQ ID:33311, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38322] Another function of VGAM1043 is therefore inhibition of KIAA1789 (Accession XM_040486). Accordingly, utilities

of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1789. KIAA1900 (Accession XM_055299) is another VGAM1043 host target gene. KIAA1900 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1900 BINDING SITE, designated SEQ ID:36260, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38323] Another function of VGAM1043 is therefore inhibition of KIAA1900 (Accession XM_055299). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1900. MGC10940 (Accession NM_032303) is another VGAM1043 host target gene. MGC10940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC10940 BINDING SITE, designated SEQ ID:26085, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38324] Another function of VGAM1043 is therefore inhibition of MGC10940 (Accession NM_032303). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10940. MGC10977 (Accession NM_032681) is another VGAM1043 host target gene. MGC10977 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10977 BINDING SITE, designated SEQ ID:26402, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38325] Another function of VGAM1043 is therefore inhibition of MGC10977 (Accession NM_032681). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10977. MGC12538 (Accession NM_032746) is another VGAM1043 host target gene. MGC12538 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC12538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12538 BINDING SITE, designated SEQ ID:26480, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38326] Another function of VGAM1043 is therefore inhibition of MGC12538 (Accession NM_032746). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12538. mPA-PLA1 (Accession NM_139248) is another VGAM1043 host target gene. mPA-PLA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by mPA-PLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of mPA-PLA1 BINDING SITE, designated SEQ ID:29252, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38327] Another function of VGAM1043 is therefore inhibition of

mPA-PLA1 (Accession NM_139248). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with mPA-PLA1. Nudix (nucleoside diphosphate linked moiety X)-type Motif 12 (NUDT12, Accession NM_031438) is another VGAM1043 host target gene. NUDT12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT12 BINDING SITE, designated SEQ ID:25449, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38328] Another function of VGAM1043 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 12 (NUDT12, Accession NM_031438). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT12. PB1 (Accession NM_018165) is another VGAM1043 host target gene. PB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PB1, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PB1 BINDING SITE, designated SEQ ID:19980, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38329] Another function of VGAM1043 is therefore inhibition of PB1 (Accession NM_018165). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PB1. SDF1 (Accession XM_165565) is another VGAM1043 host target gene. SDF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDF1 BINDING SITE, designated SEQ ID:43690, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38330] Another function of VGAM1043 is therefore inhibition of SDF1 (Accession XM_165565). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SDF1. STI2 (Accession XM_114335) is another VGAM1043 host target gene. STI2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STI2 BINDING SITE, designated SEQ ID:42877, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38331] Another function of VGAM1043 is therefore inhibition of STI2 (Accession XM_114335). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STI2. Tripartite Motif-containing 26 (TRIM26, Accession NM_003449) is another VGAM1043 host target gene. TRIM26 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIM26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM26 BINDING SITE, designated SEQ

ID:9501, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38332] Another function of VGAM1043 is therefore inhibition of Tripartite Motif-containing 26 (TRIM26, Accession NM_003449). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM26. Ubiquitin Specific Protease 8 (USP8, Accession NM_005154) is another VGAM1043 host target gene. USP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP8 BINDING SITE, designated SEQ ID:11628, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38333] Another function of VGAM1043 is therefore inhibition of Ubiquitin Specific Protease 8 (USP8, Accession NM_005154). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP8. LOC115131

(Accession NM_145242) is another VGAM1043 host target gene. LOC115131 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115131 BINDING SITE, designated SEQ ID:29756, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38334] Another function of VGAM1043 is therefore inhibition of LOC115131 (Accession NM_145242). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115131. LOC116236 (Accession XM_057674) is another VGAM1043 host target gene. LOC116236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116236 BINDING SITE, designated SEQ ID:36542, to the nucleotide sequence of VGAM1043 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3754.

[38335] Another function of VGAM1043 is therefore inhibition of LOC116236 (Accession XM_057674). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116236. LOC135398 (Accession XM_069333) is another VGAM1043 host target gene. LOC135398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135398 BINDING SITE, designated SEQ ID:37387, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38336] Another function of VGAM1043 is therefore inhibition of LOC135398 (Accession XM_069333). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135398. LOC143719 (Accession XM_027090) is another VGAM1043 host target gene. LOC143719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143719, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143719 BINDING SITE, designated SEQ ID:30404, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38337] Another function of VGAM1043 is therefore inhibition of LOC143719 (Accession XM_027090). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143719. LOC144438 (Accession XM_084860) is another VGAM1043 host target gene. LOC144438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144438 BINDING SITE, designated SEQ ID:37734, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38338] Another function of VGAM1043 is therefore inhibition of LOC144438 (Accession XM_084860). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC144438. LOC144519 (Accession XM_084890) is another VGAM1043 host target gene. LOC144519 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144519 BINDING SITE, designated SEQ ID:37756, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38339] Another function of VGAM1043 is therefore inhibition of LOC144519 (Accession XM_084890). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144519. LOC145842 (Accession XM_085254) is another VGAM1043 host target gene. LOC145842 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145842 BINDING SITE, designated SEQ ID:37996, to

the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38340] Another function of VGAM1043 is therefore inhibition of LOC145842 (Accession XM_085254). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145842. LOC145900 (Accession XM_085276) is another VGAM1043 host target gene. LOC145900 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145900 BINDING SITE, designated SEQ ID:38013, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38341] Another function of VGAM1043 is therefore inhibition of LOC145900 (Accession XM_085276). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145900. LOC145988 (Accession XM_085290) is another VGAM1043 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38041, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38342] Another function of VGAM1043 is therefore inhibition of LOC145988 (Accession XM_085290). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC146723 (Accession XM_085565) is another VGAM1043 host target gene. LOC146723 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146723, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146723 BINDING SITE, designated SEQ ID:38229, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38343] Another function of VGAM1043 is therefore inhibition of LOC146723 (Accession XM_085565). Accordingly, utilities

of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146723. LOC148266 (Accession XM_086128) is another VGAM1043 host target gene. LOC148266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148266 BINDING SITE, designated SEQ ID:38512, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38344] Another function of VGAM1043 is therefore inhibition of LOC148266 (Accession XM_086128). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148266. LOC150174 (Accession XM_086802) is another VGAM1043 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150174 BINDING SITE, designated SEQ ID:38874, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38345] Another function of VGAM1043 is therefore inhibition of LOC150174 (Accession XM_086802). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. LOC150213 (Accession XM_059324) is another VGAM1043 host target gene. LOC150213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150213 BINDING SITE, designated SEQ ID:36960, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38346] Another function of VGAM1043 is therefore inhibition of LOC150213 (Accession XM_059324). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150213. LOC152313 (Accession XM_098190) is another VGAM1043 host target gene. LOC152313 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152313 BINDING SITE, designated SEQ ID:41471, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38347] Another function of VGAM1043 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC152485 (Accession XM_087479) is another VGAM1043 host target gene. LOC152485 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152485 BINDING SITE, designated SEQ ID:39281, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38348] Another function of VGAM1043 is therefore inhibition of

LOC152485 (Accession XM_087479). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152485. LOC154860 (Accession XM_098623) is another VGAM1043 host target gene. LOC154860 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154860 BINDING SITE, designated SEQ ID:41737, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38349] Another function of VGAM1043 is therefore inhibition of LOC154860 (Accession XM_098623). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154860. LOC155006 (Accession XM_088117) is another VGAM1043 host target gene. LOC155006 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155006, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC155006 BINDING SITE, designated SEQ ID:39527, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38350] Another function of VGAM1043 is therefore inhibition of LOC155006 (Accession XM_088117). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155006. LOC158014 (Accession XM_088442) is another VGAM1043 host target gene. LOC158014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158014 BINDING SITE, designated SEQ ID:39694, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38351] Another function of VGAM1043 is therefore inhibition of LOC158014 (Accession XM_088442). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158014. LOC158056 (Accession XM_088463) is an-

other VGAM1043 host target gene. LOC158056 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158056 BINDING SITE, designated SEQ ID:39718, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38352] Another function of VGAM1043 is therefore inhibition of LOC158056 (Accession XM_088463). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158056. LOC163882 (Accession XM_089211) is another VGAM1043 host target gene. LOC163882 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163882 BINDING SITE, designated SEQ ID:39970, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38353] Another function of VGAM1043 is therefore inhibition of LOC163882 (Accession XM_089211). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163882. LOC169021 (Accession XM_095459) is another VGAM1043 host target gene. LOC169021 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169021 BINDING SITE, designated SEQ ID:40257, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38354] Another function of VGAM1043 is therefore inhibition of LOC169021 (Accession XM_095459). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169021. LOC203523 (Accession XM_114713) is another VGAM1043 host target gene. LOC203523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203523, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203523 BINDING SITE, designated SEQ ID:43054, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38355] Another function of VGAM1043 is therefore inhibition of LOC203523 (Accession XM_114713). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203523. LOC204301 (Accession XM_115306) is another VGAM1043 host target gene. LOC204301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204301 BINDING SITE, designated SEQ ID:43094, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38356] Another function of VGAM1043 is therefore inhibition of LOC204301 (Accession XM_115306). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC204301. LOC219988 (Accession XM_166223) is another VGAM1043 host target gene. LOC219988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219988 BINDING SITE, designated SEQ ID:44040, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38357] Another function of VGAM1043 is therefore inhibition of LOC219988 (Accession XM_166223). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219988. LOC220534 (Accession XM_165405) is another VGAM1043 host target gene. LOC220534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220534 BINDING SITE, designated SEQ ID:43617, to the nucleotide sequence of VGAM1043 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3754.

[38358] Another function of VGAM1043 is therefore inhibition of LOC220534 (Accession XM_165405). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220534. LOC220538 (Accession XM_165407) is another VGAM1043 host target gene. LOC220538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220538 BINDING SITE, designated SEQ ID:43627, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38359] Another function of VGAM1043 is therefore inhibition of LOC220538 (Accession XM_165407). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220538. LOC222234 (Accession XM_168558) is another VGAM1043 host target gene. LOC222234 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222234, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222234 BINDING SITE, designated SEQ ID:45240, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38360] Another function of VGAM1043 is therefore inhibition of LOC222234 (Accession XM_168558). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222234. LOC254358 (Accession XM_170771) is another VGAM1043 host target gene. LOC254358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254358 BINDING SITE, designated SEQ ID:45532, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38361] Another function of VGAM1043 is therefore inhibition of LOC254358 (Accession XM_170771). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC254358. LOC254936 (Accession XM_170770) is another VGAM1043 host target gene. LOC254936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254936 BINDING SITE, designated SEQ ID:45529, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38362] Another function of VGAM1043 is therefore inhibition of LOC254936 (Accession XM_170770). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254936. LOC257286 (Accession XM_170549) is another VGAM1043 host target gene. LOC257286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257286 BINDING SITE, designated SEQ ID:45374, to

the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38363] Another function of VGAM1043 is therefore inhibition of LOC257286 (Accession XM_170549). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257286. LOC257464 (Accession XM_116972) is another VGAM1043 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43166, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38364] Another function of VGAM1043 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC257494 (Accession XM_175212) is another VGAM1043 host target gene. LOC257494 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257494 BINDING SITE, designated SEQ ID:46688, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38365] Another function of VGAM1043 is therefore inhibition of LOC257494 (Accession XM_175212). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257494. LOC58489 (Accession XM_051862) is another VGAM1043 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35903, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38366] Another function of VGAM1043 is therefore inhibition of LOC58489 (Accession XM_051862). Accordingly, utilities

of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. LOC92017 (Accession XM_042234) is another VGAM1043 host target gene. LOC92017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92017 BINDING SITE, designated SEQ ID:33708, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38367] Another function of VGAM1043 is therefore inhibition of LOC92017 (Accession XM_042234). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92017. LOC92303 (Accession XM_044108) is another VGAM1043 host target gene. LOC92303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC92303 BINDING SITE, designated SEQ ID:34137, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38368] Another function of VGAM1043 is therefore inhibition of LOC92303 (Accession XM_044108). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92303. LOC92822 (Accession XM_047520) is another VGAM1043 host target gene. LOC92822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92822 BINDING SITE, designated SEQ ID:34986, to the nucleotide sequence of VGAM1043 RNA, herein designated VGAM RNA, also designated SEQ ID:3754.

[38369] Another function of VGAM1043 is therefore inhibition of LOC92822 (Accession XM_047520). Accordingly, utilities of VGAM1043 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92822. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1044 (VGAM1044) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38370] VGAM1044 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1044 was detected is described hereinabove with reference to Figs. 1–8.

[38371] VGAM1044 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38372] VGAM1044 gene encodes a VGAM1044 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1044 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1044 precursor RNA is designated SEQ ID:1030, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1030 is located at position 131364 relative to the

genome of Human Herpesvirus 8.

[38373] VGAM1044 precursor RNA folds onto itself, forming VGAM1044 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38374] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1044 folded precursor RNA into VGAM1044 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1044 RNA is designated SEQ ID:3755, and is provided hereinbelow with reference to the sequence listing part.

[38375] VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1044 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38376] VGAM1044 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1044 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1044 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38377] The complementary binding of VGAM1044 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1044 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1044 host target RNA into VGAM1044 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38378] It is appreciated that VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1044 host target genes. The mRNA of each one of this plurality of VGAM1044 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1044 RNA, herein designated VGAM RNA, and which when bound by VGAM1044 RNA causes inhibition of translation of respective one or more VGAM1044 host target proteins.

[38379] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1044 gene, herein designated VGAM GENE, on one or more VGAM1044 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38380] It is yet further appreciated that a function of VGAM1044 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1044

correlate with, and may be deduced from, the identity of the host target genes which VGAM1044 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38381] Nucleotide sequences of the VGAM1044 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1044 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1044 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1044 are further described hereinbelow with reference to Table 1.

[38382] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1044 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1044 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38383] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1044 gene, herein designated VGAM is inhibition of expression of VGAM1044 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1044 correlate with, and may be deduced

from, the identity of the target genes which VGAM1044 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38384] Aldehyde Dehydrogenase 1 Family, Member A3

(ALDH1A3, Accession NM_000693) is a VGAM1044 host target gene. ALDH1A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH1A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH1A3 BINDING SITE, designated SEQ ID:6353, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38385] A function of VGAM1044 is therefore inhibition of Aldehyde Dehydrogenase 1 Family, Member A3 (ALDH1A3, Accession NM_000693), a gene which plays a major role in the detoxification of aldehydes generated by alcohol metabolism and lipid peroxidation. Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH1A3. The function of ALDH1A3 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM565.UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 1 (B4GALT1, Accession NM_001497) is another VGAM1044 host target gene. B4GALT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT1 BINDING SITE, designated SEQ ID:7244, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38386] Another function of VGAM1044 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 1 (B4GALT1, Accession NM_001497). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT1. Prokineticin 1 (PROK1, Accession NM_032414) is another VGAM1044 host target gene. PROK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROK1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROK1 BINDING SITE, designated SEQ ID:26197, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38387] Another function of VGAM1044 is therefore inhibition of Prokineticin 1 (PROK1, Accession NM_032414), a gene which induces proliferation, migration and fenestration in capillary endothelial cells derived from endocrine glands. Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROK1. The function of PROK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1000. Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630) is another VGAM1044 host target gene. SLC21A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SLC21A2 BINDING SITE, designated SEQ ID:12158, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38388] Another function of VGAM1044 is therefore inhibition of Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630), a gene which is a Prostaglandin transporter. Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A2. The function of SLC21A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83.Unc-119 Homolog (*C. elegans*) (UNC119, Accession NM_005148) is another VGAM1044 host target gene. UNC119 BINDING SITE1 and UNC119 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UNC119, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC119 BINDING SITE1 and UNC119 BINDING SITE2, designated SEQ ID:11620 and SEQ ID:27646 respectively,

to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38389] Another function of VGAM1044 is therefore inhibition of Unc-119 Homolog (*C. elegans*) (UNC119, Accession NM_005148), a gene which is expressed in the retina and may play a role in the mechanism of photoreceptor neurotransmitter release through the synaptic vesicle cycle. Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC119. The function of UNC119 has been established by previous studies. Using a subtractive hybridization strategy, Higashide et al. (1996) identified a retina-specific cDNA that they designated HRG4 (human retinal gene-4). Northern blot analysis revealed that the approximately 1.4-kb HRG4 mRNA is expressed specifically in human retina. The authors also cloned a cDNA encoding RRG4, the rat HRG4 homolog. The predicted 240-amino acid human and rat proteins both contain an N-terminal region rich in proline and glycine followed by a region with a mixture of alpha helices, beta sheets, and turns. Sequence comparisons indicated that the proline-glycine domains of RRG4 and HRG4 share only 67% homology, while the rest of the sequence

is 100% identical. By in situ hybridization, Higashide et al. (1996) demonstrated that the HRG4 gene is expressed specifically in photoreceptors, both rods and cones, in human retina. In rat, the authors observed high levels of RRG4 expression in the outer retina beginning around postnatal day 5, when the photoreceptors begin to differentiate, and expression increased rapidly to reach the adult level by postnatal day 23. Mutations in the *C. elegans* *unc119* gene lead to defects in locomotion, feeding behavior, and chemosensation. Both Swanson et al. (1998) and Higashide et al. (1998) observed that HRG4 shares strong homology with the *C. elegans* *unc119* protein, leading Swanson et al. (1998) to designate the human protein UNC119. Swanson et al. (1998) stated that a human UNC119 cDNA functionally complemented the *C. elegans* *unc119* mutation. Using immunofluorescence, Higashide et al. (1998) localized HRG4 to the outer plexiform layer of the retina in the synaptic termini of rod and cone photoreceptors. Electron microscopic immunolocalization showed that the protein is present in the cytoplasm and on the presynaptic membranes of the photoreceptor synapses. The authors suggested that HRG4 may play a role in the mechanism of photoreceptor neuro-

transmitter release through the synaptic vesicle cycle. They noted that the homology of HRG4 and unc119 is consistent with a possible role of HRG4 in the synaptic vesicle cycle, because the broad effects of unc119 on neuronal function are consistent with a defect in neurotransmission.

[38390] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38391] Higashide, T.; Murakami, A.; McLaren, M. J.; Inana, G. : Cloning of the cDNA for a novel photoreceptor protein. J. Biol. Chem. 271: 1797–1804, 1996. ; and

[38392] Swanson, D. A.; Chang, J. T.; Campochiaro, P. A.; Zack, D. J.; Valle, D. : Mammalian orthologs of *C. elegans* unc-119 highly expressed in photoreceptors. Invest. Ophthalm. Vis. Sci. 39: 20.

[38393] Further studies establishing the function and utilities of UNC119 are found in John Hopkins OMIM database record ID 604011, and in cited publications numbered 7608–7611 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Double C2-like Domains, Beta (DOC2B, Accession NM_003585) is another VGAM1044 host target gene. DOC2B BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DOC2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOC2B BINDING SITE, designated SEQ ID:9636, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38394] Another function of VGAM1044 is therefore inhibition of Double C2-like Domains, Beta (DOC2B, Accession NM_003585). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOC2B. KIAA0767 (Accession XM_027105) is another VGAM1044 host target gene. KIAA0767 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0767, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0767 BINDING SITE, designated SEQ ID:30407, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38395] Another function of VGAM1044 is therefore inhibition of KIAA0767 (Accession XM_027105). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0767. KIAA1297 (Accession XM_051005) is another VGAM1044 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35711, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38396] Another function of VGAM1044 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1822 (Accession XM_041566) is another VGAM1044 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33554, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38397] Another function of VGAM1044 is therefore inhibition of KIAA1822 (Accession XM_041566). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. NRF (Accession NM_017544) is another VGAM1044 host target gene. NRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRF BINDING SITE, designated SEQ ID:18984, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38398] Another function of VGAM1044 is therefore inhibition of NRF (Accession NM_017544). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRF.

Tubby Homolog (mouse) (TUB, Accession NM_003320) is another VGAM1044 host target gene. TUB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUB BINDING SITE, designated SEQ ID:9322, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38399] Another function of VGAM1044 is therefore inhibition of Tubby Homolog (mouse) (TUB, Accession NM_003320). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUB. LOC127702 (Accession XM_060619) is another VGAM1044 host target gene. LOC127702 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127702, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127702 BINDING SITE, designated SEQ ID:37180, to the nucleotide sequence of

VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38400] Another function of VGAM1044 is therefore inhibition of LOC127702 (Accession XM_060619). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127702. LOC150407 (Accession XM_086906) is another VGAM1044 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38950, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38401] Another function of VGAM1044 is therefore inhibition of LOC150407 (Accession XM_086906). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC166341 (Accession XM_093804) is another VGAM1044 host target gene. LOC166341 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC166341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166341 BINDING SITE, designated SEQ ID:40210, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38402] Another function of VGAM1044 is therefore inhibition of LOC166341 (Accession XM_093804). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166341. LOC219942 (Accession XM_167790) is another VGAM1044 host target gene. LOC219942 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219942 BINDING SITE, designated SEQ ID:44824, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38403] Another function of VGAM1044 is therefore inhibition of LOC219942 (Accession XM_167790). Accordingly, utilities

of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219942. LOC253868 (Accession XM_170975) is another VGAM1044 host target gene. LOC253868 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253868 BINDING SITE, designated SEQ ID:45751, to the nucleotide sequence of VGAM1044 RNA, herein designated VGAM RNA, also designated SEQ ID:3755.

[38404] Another function of VGAM1044 is therefore inhibition of LOC253868 (Accession XM_170975). Accordingly, utilities of VGAM1044 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253868. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1045 (VGAM1045) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38405] VGAM1045 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1045 was detected is described hereinabove with reference to Figs. 1–8.

[38406] VGAM1045 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sulfolobus Virus SIRV–1. VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38407] VGAM1045 gene encodes a VGAM1045 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1045 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1045 precursor RNA is designated SEQ ID:1031, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1031 is located at position 26929 relative to the genome of Sulfolobus Virus SIRV–1.

[38408] VGAM1045 precursor RNA folds onto itself, forming VGAM1045 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38409] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1045 folded precursor RNA into VGAM1045 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1045 RNA is designated SEQ ID:3756, and is provided hereinbelow with reference to the sequence listing part.

[38410] VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1045 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[38411] VGAM1045 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1045 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1045 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38412] The complementary binding of VGAM1045 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1045 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1045 host target RNA into VGAM1045 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38413] It is appreciated that VGAM1045 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1045 host target genes. The mRNA of each one of this plurality of VGAM1045 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1045 RNA, herein designated VGAM RNA, and which when bound by VGAM1045 RNA causes inhibition of translation of respective one or more VGAM1045 host target proteins.

[38414] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1045 gene, herein designated VGAM GENE, on one or more VGAM1045 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38415] It is yet further appreciated that a function of VGAM1045 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of viral infection by Sulfolobus Virus SIRV-1. Specific functions, and accordingly utilities, of VGAM1045 correlate with, and may be deduced from, the identity of the host target genes which VGAM1045 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38416] Nucleotide sequences of the VGAM1045 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1045 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1045 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1045 are further
described hereinbelow with reference to Table 1.

[38417] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1045 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1045 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[38418] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1045 gene, herein designated VGAM is
inhibition of expression of VGAM1045 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1045 correlate with, and may be deduced
from, the identity of the target genes which VGAM1045
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[38419] Enamelin (ENAM, Accession NM_031889) is a VGAM1045
host target gene. ENAM BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by ENAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAM BINDING SITE, designated SEQ ID:25633, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38420] A function of VGAM1045 is therefore inhibition of Enamelin (ENAM, Accession NM_031889). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAM. MAX Interacting Protein 1 (MXI1, Accession NM_005962) is another VGAM1045 host target gene. MXI1 BINDING SITE1 and MXI1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MXI1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MXI1 BINDING SITE1 and MXI1 BINDING SITE2, designated SEQ ID:12585 and SEQ ID:28195 respectively, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3756.

[38421] Another function of VGAM1045 is therefore inhibition of MAX Interacting Protein 1 (MXI1, Accession NM_005962), a gene which acts as a tumor suppressor in vivo, engages the MYC network in a functionally relevant manner. Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MXI1. The function of MXI1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Rabphilin 3A-like (without C2 domains) (RPH3AL, Accession NM_006987) is another VGAM1045 host target gene. RPH3AL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPH3AL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPH3AL BINDING SITE, designated SEQ ID:13847, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38422] Another function of VGAM1045 is therefore inhibition of Rabphilin 3A-like (without C2 domains) (RPH3AL, Acces-

sion NM_006987), a gene which is a protein transporter. could play a role in neurotransmitter release by regulating membrane flow in the nerve terminal. Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPH3AL. The function of RPH3AL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. FHR5 (Accession NM_030787) is another VGAM1045 host target gene. FHR5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHR5 BINDING SITE, designated SEQ ID:25085, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38423] Another function of VGAM1045 is therefore inhibition of FHR5 (Accession NM_030787). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHR5. FLJ10922 (Accession NM_018273) is another VGAM1045

host target gene. FLJ10922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10922 BINDING SITE, designated SEQ ID:20257, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38424] Another function of VGAM1045 is therefore inhibition of FLJ10922 (Accession NM_018273). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10922. FLJ20730 (Accession NM_017945) is another VGAM1045 host target gene. FLJ20730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20730 BINDING SITE, designated SEQ ID:19642, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38425] Another function of VGAM1045 is therefore inhibition of FLJ20730 (Accession NM_017945). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20730. FLJ21820 (Accession NM_021925) is another VGAM1045 host target gene. FLJ21820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21820 BINDING SITE, designated SEQ ID:22453, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38426] Another function of VGAM1045 is therefore inhibition of FLJ21820 (Accession NM_021925). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21820. ICK (Accession NM_014920) is another VGAM1045 host target gene. ICK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICK BINDING SITE, designated SEQ ID:17197, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38427] Another function of VGAM1045 is therefore inhibition of ICK (Accession NM_014920). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICK. IPLA2(GAMMA) (Accession XM_027224) is another VGAM1045 host target gene. IPLA2(GAMMA) BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IPLA2(GAMMA), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IPLA2(GAMMA) BINDING SITE, designated SEQ ID:30446, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38428] Another function of VGAM1045 is therefore inhibition of IPLA2(GAMMA) (Accession XM_027224). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with IPLA2(GAMMA). KIAA0276 (Accession XM_048199) is another VGAM1045 host target gene. KIAA0276 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0276 BINDING SITE, designated SEQ ID:35136, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38429] Another function of VGAM1045 is therefore inhibition of KIAA0276 (Accession XM_048199). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0276. moblak (Accession NM_130807) is another VGAM1045 host target gene. moblak BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by moblak, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of moblak BINDING SITE, designated SEQ ID:28311, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA,

also designated SEQ ID:3756.

[38430] Another function of VGAM1045 is therefore inhibition of moblak (Accession NM_130807). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with moblak. LOC221760 (Accession XM_168105) is another VGAM1045 host target gene. LOC221760 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221760 BINDING SITE, designated SEQ ID:45032, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38431] Another function of VGAM1045 is therefore inhibition of LOC221760 (Accession XM_168105). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221760. LOC257422 (Accession XM_172923) is another VGAM1045 host target gene. LOC257422 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257422, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257422 BINDING SITE, designated SEQ ID:46189, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38432] Another function of VGAM1045 is therefore inhibition of LOC257422 (Accession XM_172923). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257422. LOC90459 (Accession XM_031826) is another VGAM1045 host target gene. LOC90459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90459 BINDING SITE, designated SEQ ID:31492, to the nucleotide sequence of VGAM1045 RNA, herein designated VGAM RNA, also designated SEQ ID:3756.

[38433] Another function of VGAM1045 is therefore inhibition of LOC90459 (Accession XM_031826). Accordingly, utilities of VGAM1045 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90459. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1046 (VGAM1046) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38434] VGAM1046 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1046 was detected is described hereinabove with reference to Figs. 1–8.

[38435] VGAM1046 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 8. VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38436] VGAM1046 gene encodes a VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1046 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1046 precursor RNA is desig-

nated SEQ ID:1032, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1032 is located at position 131131 relative to the genome of Human Herpesvirus 8.

- [38437] VGAM1046 precursor RNA folds onto itself, forming VGAM1046 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38438] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1046 folded precursor RNA into VGAM1046 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1046 RNA is designated SEQ ID:3757, and is provided hereinbelow with reference to the sequence

listing part.

[38439] VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1046 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38440] VGAM1046 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1046 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1046 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38441] The complementary binding of VGAM1046 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1046 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1046 host target RNA into VGAM1046 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38442] It is appreciated that VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1046 host target genes. The mRNA of each one of this plurality of VGAM1046 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1046 RNA, herein designated VGAM

RNA, and which when bound by VGAM1046 RNA causes inhibition of translation of respective one or more VGAM1046 host target proteins.

[38443] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1046 gene, herein designated VGAM GENE, on one or more VGAM1046 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38444] It is yet further appreciated that a function of VGAM1046 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1046 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGAM1046 correlate with, and may be deduced from, the identity of the host target genes which VGAM1046 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38445] Nucleotide sequences of the VGAM1046 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1046 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1046 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1046 are further described hereinbelow with reference to Table 1.

[38446] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1046 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1046 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38447] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1046 gene, herein designated VGAM is

inhibition of expression of VGAM1046 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1046 correlate with, and may be deduced from, the identity of the target genes which VGAM1046 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38448] Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218) is a VGAM1046 host target gene. KCNQ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNQ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNQ1 BINDING SITE, designated SEQ ID:5721, to the nucleotide sequence of VGAM1046 RNA, herein designated VGAM RNA, also designated SEQ ID:3757.

[38449] A function of VGAM1046 is therefore inhibition of Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218), a gene which probably important in cardiac repolarization. associates with kcne1 (mink) to form the i(ks) cardiac potassium current. elicits a rapidly activating, k(+)-selective outward

current. muscarinic agonist oxotremorine-m strongly suppresses kcnq1/kcne1 current in cho cells in which cloned kcnq1/kcne1 channels were coexpressed with m1 muscarinic receptors. may associate also with kcne3 (mirp2) to form the potassium channel that is important for cyclic amp-stimulated intestinal secretion of chloride

io TISSUE:abondantly expressed in heart, pancreas, prostate, kidney, small intestine and peripheral blood leukocytes. less abundant in placenta, lung, spleen, colon, thymus, testis and ovaries. Accordingly, utilities of VGAM1046 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNQ1. The function of KCNQ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM339.DKFZP761D0211 (Accession NM_032039) is another VGAM1046 host target gene. DKFZP761D0211 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DK-FZP761D0211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761D0211 BINDING SITE,

designated SEQ ID:25735, to the nucleotide sequence of VGAM1046 RNA, herein designated VGAM RNA, also designated SEQ ID:3757.

[38450] Another function of VGAM1046 is therefore inhibition of DKFZP761D0211 (Accession NM_032039). Accordingly, utilities of VGAM1046 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761D0211. LOC149132 (Accession XM_086428) is another VGAM1046 host target gene. LOC149132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149132 BINDING SITE, designated SEQ ID:38643, to the nucleotide sequence of VGAM1046 RNA, herein designated VGAM RNA, also designated SEQ ID:3757.

[38451] Another function of VGAM1046 is therefore inhibition of LOC149132 (Accession XM_086428). Accordingly, utilities of VGAM1046 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149132. LOC255975 (Accession XM_171083) is an-

other VGAM1046 host target gene. LOC255975 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255975 BINDING SITE, designated SEQ ID:45887, to the nucleotide sequence of VGAM1046 RNA, herein designated VGAM RNA, also designated SEQ ID:3757.

[38452] Another function of VGAM1046 is therefore inhibition of LOC255975 (Accession XM_171083). Accordingly, utilities of VGAM1046 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255975. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1047 (VGAM1047) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38453] VGAM1047 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1047 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[38454] VGAM1047 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mild Yellow Edge Virus. VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38455] VGAM1047 gene encodes a VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1047 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1047 precursor RNA is designated SEQ ID:1033, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1033 is located at position 3766 relative to the genome of Strawberry Mild Yellow Edge Virus.

[38456] VGAM1047 precursor RNA folds onto itself, forming VGAM1047 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38457] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1047 folded precursor RNA into VGAM1047 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1047 RNA is designated SEQ ID:3758, and is provided hereinbelow with reference to the sequence listing part.

[38458] VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1047 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38459] VGAM1047 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1047 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1047 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1047 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38460] The complementary binding of VGAM1047 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1047 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1047 host target RNA into VGAM1047 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38461] It is appreciated that VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1047 host target genes. The mRNA of each one of this plurality of VGAM1047 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1047 RNA, herein designated VGAM RNA, and which when bound by VGAM1047 RNA causes inhibition of translation of respective one or more VGAM1047 host target proteins.

[38462] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1047 gene, herein designated VGAM GENE, on one or more VGAM1047 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38463] It is yet further appreciated that a function of VGAM1047 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of viral infection by Strawberry Mild Yellow Edge Virus. Specific functions, and accordingly utilities, of VGAM1047 correlate with, and may be deduced from, the identity of the host target genes which VGAM1047 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38464] Nucleotide sequences of the VGAM1047 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1047 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1047 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1047 are further described hereinbelow with reference to Table 1.

[38465] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1047 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1047 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38466] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1047 gene, herein designated VGAM is inhibition of expression of VGAM1047 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1047 correlate with, and may be deduced from, the identity of the target genes which VGAM1047 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38467] Homeo Box C13 (HOXC13, Accession XM_006804) is a VGAM1047 host target gene. HOXC13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXC13 BINDING SITE, designated SEQ ID:30016, to the nucleotide sequence of VGAM1047 RNA, herein designated VGAM RNA, also designated SEQ ID:3758.

[38468] A function of VGAM1047 is therefore inhibition of Homeo Box C13 (HOXC13, Accession XM_006804). Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXC13. P53AIP1 (Accession NM_022112) is another VGAM1047 host target gene. P53AIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P53AIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P53AIP1 BINDING SITE, designated SEQ ID:22658, to the nucleotide sequence of VGAM1047 RNA, herein designated VGAM RNA, also designated SEQ ID:3758.

[38469] Another function of VGAM1047 is therefore inhibition of P53AIP1 (Accession NM_022112). Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

P53AIP1. Vinculin (VCL, Accession NM_003373) is another VGAM1047 host target gene. VCL BINDING SITE1 and VCL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by VCL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VCL BINDING SITE1 and VCL BINDING SITE2, designated SEQ ID:9403 and SEQ ID:15192 respectively, to the nucleotide sequence of VGAM1047 RNA, herein designated VGAM RNA, also designated SEQ ID:3758.

[38470] Another function of VGAM1047 is therefore inhibition of Vinculin (VCL, Accession NM_003373). Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VCL. MGC11242 (Accession NM_024320) is another VGAM1047 host target gene. MGC11242 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11242 BINDING SITE, designated SEQ ID:23610, to

the nucleotide sequence of VGAM1047 RNA, herein designated VGAM RNA, also designated SEQ ID:3758.

[38471] Another function of VGAM1047 is therefore inhibition of MGC11242 (Accession NM_024320). Accordingly, utilities of VGAM1047 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11242. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1048 (VGAM1048) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38472] VGAM1048 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1048 was detected is described hereinabove with reference to Figs. 1–8.

[38473] VGAM1048 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mild Yellow Edge Virus. VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38474] VGAM1048 gene encodes a VGAM1048 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1048 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1048 precursor RNA is designated SEQ ID:1034, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1034 is located at position 1114 relative to the genome of Strawberry Mild Yellow Edge Virus.

[38475] VGAM1048 precursor RNA folds onto itself, forming VGAM1048 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38476] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1048 folded precursor RNA into VGAM1048 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1048 RNA is designated SEQ ID:3759, and is provided hereinbelow with reference to the sequence listing part.

[38477] VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1048 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38478] VGAM1048 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1048 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1048 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38479] The complementary binding of VGAM1048 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1048 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1048 host target RNA into VGAM1048 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38480] It is appreciated that VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1048 host target genes. The mRNA of each one of this plurality of VGAM1048 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1048 RNA, herein designated VGAM RNA, and which when bound by VGAM1048 RNA causes inhibition of translation of respective one or more VGAM1048 host target proteins.

[38481] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1048 gene, herein designated VGAM GENE, on one or more VGAM1048 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[38482] It is yet further appreciated that a function of VGAM1048 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of viral infection by Strawberry Mild Yellow Edge Virus. Specific functions, and accordingly utilities, of VGAM1048 correlate with, and may be deduced from, the identity of the host target genes which VGAM1048 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38483] Nucleotide sequences of the VGAM1048 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1048 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1048 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1048 are further described hereinbelow with reference to Table 1.

[38484] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1048 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1048 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38485] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1048 gene, herein designated VGAM is inhibition of expression of VGAM1048 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1048 correlate with, and may be deduced from, the identity of the target genes which VGAM1048 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38486] Adaptor-related Protein Complex 1, Beta 1 Subunit (AP1B1, Accession NM_001127) is a VGAM1048 host target gene. AP1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1B1 BINDING SITE, designated SEQ ID:6797, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38487] A function of VGAM1048 is therefore inhibition of Adap-

tor-related Protein Complex 1, Beta 1 Subunit (AP1B1, Accession NM_001127), a gene which plays a role in protein sorting in the late-golgi/trans-golgi network (tgn) and/or endosomes. Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1B1. The function of AP1B1 has been established by previous studies. A 140-kb homozygous deletion in 22q12 in a sporadic meningioma directed Peyrard et al. (1994) to the cloning and characterization of a new member of the human beta-adaptin gene family, which was named BAM22 for 'beta-adaptin-meningioma-chromosome 22.' The BAM22 gene was totally inactivated in the tumor with homozygous deletion. Northern blot analysis of 70 sporadic meningiomas showed specific loss of expression in 8 tumors, suggesting inactivation of BAM22. Based on this, Peyrard et al. (1994) suggested that BAM22 is a second chromosome 22 locus important in meningioma development and second in importance to the neurofibromatosis type 2 gene (NF2; 101000). The likelihood that multiple loci on chromosome 22 are involved in the oncogenesis of meningioma is suggested by the facts that monosomy 22 is observed in as many as 65% of tumors (Zankl and Zang,

1980); some meningiomas have chromosome 22 deletions not encompassing the NF2 gene region and do not show mutations in the NF2 gene; and constitutional ring chromosome 22 has been observed in young patients with multiple tumors (Arinami et al., 1986; Petrella et al., 1993).

[38488] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38489] Peyrard, M.; Pan, H.-Q.; Kedra, D.; Fransson, I.; Swahn, S.; Hartman, K.; Clifton, S. W.; Roe, B. A.; Dumanski, J. P. : Structure of the promoter and genomic organization of the human beta-prime-adaptin gene (BAM22) from chromosome 22q12. Genomics 36: 112-117, 1996. ; and

[38490] Zankl, H.; Zang, K. D. : Correlations between clinical and cytogenetical data in 180 human meningiomas. Cancer Genet. Cytogenet. 1: 351-356, 1980.

[38491] Further studies establishing the function and utilities of AP1B1 are found in John Hopkins OMIM database record ID 600157, and in cited publications numbered 754 and 12596-7550 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Piccolo (presynaptic cytomatrix protein) (PCLO, Ac-

cession XM_168530) is another VGAM1048 host target gene. PCLO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCLO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCLO BINDING SITE, designated SEQ ID:45213, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38492] Another function of VGAM1048 is therefore inhibition of Piccolo (presynaptic cytomatrix protein) (PCLO, Accession XM_168530), a gene which involves in the cycling of synaptic vesicles. Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCLO. The function of PCLO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. TRHDE (Accession NM_013381) is another VGAM1048 host target gene. TRHDE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRHDE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TRHDE BINDING SITE, designated SEQ ID:15032, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38493] Another function of VGAM1048 is therefore inhibition of TRHDE (Accession NM_013381). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRHDE. FLJ10932 (Accession NM_018277) is another VGAM1048 host target gene. FLJ10932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10932 BINDING SITE, designated SEQ ID:20262, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38494] Another function of VGAM1048 is therefore inhibition of FLJ10932 (Accession NM_018277). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10932. KIAA0349 (Accession XM_166449) is another VGAM1048 host target gene. KIAA0349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0349 BINDING SITE, designated SEQ ID:44338, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38495] Another function of VGAM1048 is therefore inhibition of KIAA0349 (Accession XM_166449). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0349. KIAA1954 (Accession XM_085375) is another VGAM1048 host target gene. KIAA1954 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1954 BINDING SITE, designated SEQ ID:38097, to the nucleotide sequence of VGAM1048 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3759.

[38496] Another function of VGAM1048 is therefore inhibition of KIAA1954 (Accession XM_085375). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1954. LOC148443 (Accession XM_086196) is another VGAM1048 host target gene. LOC148443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148443 BINDING SITE, designated SEQ ID:38538, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38497] Another function of VGAM1048 is therefore inhibition of LOC148443 (Accession XM_086196). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148443. LOC149506 (Accession XM_097661) is another VGAM1048 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149506, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41010, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38498] Another function of VGAM1048 is therefore inhibition of LOC149506 (Accession XM_097661). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149506. LOC157556 (Accession XM_098783) is another VGAM1048 host target gene. LOC157556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157556 BINDING SITE, designated SEQ ID:41819, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38499] Another function of VGAM1048 is therefore inhibition of LOC157556 (Accession XM_098783). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC157556. LOC203427 (Accession XM_114699) is another VGAM1048 host target gene. LOC203427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203427 BINDING SITE, designated SEQ ID:43043, to the nucleotide sequence of VGAM1048 RNA, herein designated VGAM RNA, also designated SEQ ID:3759.

[38500] Another function of VGAM1048 is therefore inhibition of LOC203427 (Accession XM_114699). Accordingly, utilities of VGAM1048 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203427. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1049 (VGAM1049) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38501] VGAM1049 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1049 was detected is described hereinabove with reference to Figs. 1–8.

[38502] VGAM1049 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mild Yellow Edge Virus. VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38503] VGAM1049 gene encodes a VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1049 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1049 precursor RNA is designated SEQ ID:1035, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1035 is located at position 4885 relative to the genome of Strawberry Mild Yellow Edge Virus.

[38504] VGAM1049 precursor RNA folds onto itself, forming VGAM1049 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38505] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1049 folded precursor RNA into VGAM1049 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1049 RNA is designated SEQ ID:3760, and is provided hereinbelow with reference to the sequence listing part.

[38506] VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1049 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38507] VGAM1049 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1049 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1049 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38508] The complementary binding of VGAM1049 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1049 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1049 host target RNA into VGAM1049 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38509] It is appreciated that VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1049 host target genes. The mRNA of each one of this plurality of VGAM1049 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1049 RNA, herein designated VGAM RNA, and which when bound by VGAM1049 RNA causes inhibition of translation of respective one or more VGAM1049 host target proteins.

[38510] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1049 gene, herein designated VGAM GENE, on one or more VGAM1049 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38511] It is yet further appreciated that a function of VGAM1049 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of viral infection by Strawberry Mild Yellow Edge Virus. Specific functions, and accordingly utilities, of VGAM1049 correlate with, and may be deduced from, the identity of the host target genes which VGAM1049 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38512] Nucleotide sequences of the VGAM1049 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1049 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1049 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1049 are further described hereinbelow with reference to Table 1.

[38513] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1049 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1049 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38514] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1049 gene, herein designated VGAM is inhibition of expression of VGAM1049 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1049 correlate with, and may be deduced from, the identity of the target genes which VGAM1049 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38515] Solute Carrier Family 39 (zinc transporter), Member 1 (SLC39A1, Accession NM_014437) is a VGAM1049 host target gene. SLC39A1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by SLC39A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC39A1 BINDING SITE, designated SEQ ID:15793, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38516] A function of VGAM1049 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 1 (SLC39A1, Accession NM_014437), a gene which is a divalent (zinc/iron) metal ion transporter. Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC39A1. The function of SLC39A1 has been established by previous studies. The ZRT- and IRT-related protein (ZIP) family is composed of divalent metal ion transporters, including *A. thaliana* IRT1 (iron-regulated transporter-1), which appears to play a role in iron uptake, and *S. cerevisiae* ZRT1 (zinc-regulated transporter-1) and ZRT2, and *A. thaliana* ZIP1 to ZIP4, all of which are probably zinc transporters (reviewed by Eng et al., 1998). The human growth arrest-inducible gene product (GAIP) is

also a ZIP family member based on sequence similarity. Lioumi et al. (1998) generated a transcript map of the region within and in the proximity of the epidermal differentiation complex (EDC; 601588), which is located in 1q21. They identified a partial ZIRTL cDNA as mapping to the distal end of the EDC, 200 kb from the S100A1 gene (OMIM Ref. No. 176940). Lioumi et al. (1998) found that a portion of the ZIRTL cDNA encodes a polypeptide with significant sequence similarity to the ZIP family of iron and zinc transporters from plants and yeast. By screening a human keratinocyte cDNA library with the partial ZIRTL cDNA, Lioumi et al. (1999) isolated a full-length ZIRTL cDNA. The predicted 324-amino acid ZIRTL protein contains 8 transmembrane domains, 9 possible N-myristylation sites, a potential protein kinase C phosphorylation site, and 4 potential protein kinase II phosphorylation sites. Human ZIRTL shares 21 to 22% amino acid sequence identity with *A. thaliana* IRT1 and ZIP1 to ZIP4, *Pisum sativum* Rit1, and *S. cerevisiae* ZRT1 and ZRT2. ZIRTL also shares 34% amino acid sequence identity with GAIP. The human and mouse Zirtl proteins are 90% similar. The ZIRTL gene contains 4 exons. Northern blot analysis detected a 2.1-kb ZIRTL transcript in all human tis-

sues tested, namely adult heart, lung, brain, liver, pancreas, small intestine, colon, kidney, spleen, thymus, peripheral blood leukocytes, skeletal muscle, testis, ovary, placenta, prostate, and keratinocytes, and fetal heart, kidney, small intestine, and skin. In situ hybridization showed that mouse Zirtl is developmentally regulated in the skin, where it was expressed in the epidermal layer, excluding the dermis, at E17.5, but not in embryonic days 10.5 and 15.5 or P21. In the small intestine, Zirtl was found toward the base of the intestinal villi from E17.5. In the pancreas, Zirtl expression was found from E17.5. Zirtl expression was not detected in the liver. Zirtl was expressed in osteoblasts of developing bone from E15.5 and in ameloblasts and odontoblasts at late stages of tooth development at P21. Moderate expression of Zirtl was observed in brain in the hippocampus

[38517] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38518] Lioumi, M.; Ferguson, C. A.; Sharpe, P. T.; Freeman, T.; Marenholz, I.; Mischke, D.; Heizmann, C.; Ragoussis, J. : Isolation and characterization of human and mouse ZIRTL, a member of the IRT1 family of transporters, mapping

within the epidermal differentiation complex. Genomics 62: 272–280, 1999. ; and

[38519] Lioumi, M.; Olavesen, M. G.; Nizetic, D.; Ragoussis, J. : High-resolution YAC fragmentation map of 1q21. Genomics 49: 200–208, 1998.

[38520] Further studies establishing the function and utilities of SLC39A1 are found in John Hopkins OMIM database record ID 604740, and in cited publications numbered 6744–6746 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Spastic Paraplegia 4 (autosomal dominant; spastin) (SPG4, Accession NM_014946) is another VGAM1049 host target gene. SPG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPG4 BINDING SITE, designated SEQ ID:17261, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38521] Another function of VGAM1049 is therefore inhibition of Spastic Paraplegia 4 (autosomal dominant; spastin) (SPG4, Accession NM_014946), a gene which is probably an AT–

Pase involved in the assembly or function of nuclear protein complexes. Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPG4. The function of SPG4 has been established by previous studies. SPG4 is ubiquitously expressed in human adult and fetal tissue, showing slightly higher expression in fetal brain. Hazan et al. (1999) cloned the mouse ortholog of SPG4, which between amino acids 113 and 616 has 96% identity with human SPG4. Spg4 transcripts are ubiquitously expressed in adult tissues and from embryonic day 7 to 17 in mouse. Interaction with the cytoskeleton was mediated by the N-terminal region of spastin and was regulated through the ATPase activity of the AAA domain. Expression of missense mutations (including 604277.0001, 604277.0002, and 604277.0004) into the AAA domain led to constitutive binding to microtubules in transfected cells and induced the disappearance of the aster and the formation of thick perinuclear bundles, suggesting a role of spastin in microtubule dynamics. Consistently, wildtype spastin promoted microtubule disassembly in transfected cells. The authors suggested that spastin may be involved in microtubule dynamics similarly to the highly homologous mi-

crotubule-severing protein katanin (OMIM Ref. No. 606696). The authors hypothesized that impairment of fine regulation of the microtubule cytoskeleton in long axons, due to spastin mutations, may underlie the pathogenesis of hereditary spastic paraplegia

[38522] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38523] Hazan, J.; Fonknechten, N.; Mavel, D.; Paternotte, C.; Samson, D.; Artiguenave, F.; Davoine, C.-S.; Cruaud, C.; Durr, A.; Wincker, P.; Brottier, P.; Cattolico, L.; Barbe, V.; Burgunder, J.-M.; Prud'homme, J.-F.; Brice, A.; Fontaine, B.; Heilig, R.; Weissenbach, J. : Spastin, a new AAA protein, is altered in the most frequent form of autosomal dominant spastic paraplegia. *Nature Genet.* 23: 296-303, 1999. ; and

[38524] Errico, A.; Ballabio, A.; Rugarli, E. I. : Spastin, the protein mutated in autosomal dominant hereditary spastic paraplegia, is involved in microtubule dynamics. *Hum. Molec. Genet.* 11: 153.

[38525] Further studies establishing the function and utilities of SPG4 are found in John Hopkins OMIM database record ID 604277, and in cited publications numbered

10496–7390, 10497–7396, 7391, 10498–761 and 10499 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434A043 (Accession NM_015396) is another VGAM1049 host target gene. DKFZP434A043 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434A043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434A043 BINDING SITE, designated SEQ ID:17702, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38526] Another function of VGAM1049 is therefore inhibition of DKFZP434A043 (Accession NM_015396). Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434A043. FLJ12526 (Accession NM_024787) is another VGAM1049 host target gene. FLJ12526 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12526, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ12526 BINDING SITE, designated SEQ ID:24168, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38527] Another function of VGAM1049 is therefore inhibition of FLJ12526 (Accession NM_024787). Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12526. KIAA0513 (Accession NM_014732) is another VGAM1049 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16358, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38528] Another function of VGAM1049 is therefore inhibition of KIAA0513 (Accession NM_014732). Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. Placenta-specific 3 (PLAC3, Accession

XM_045115) is another VGAM1049 host target gene.

PLAC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC3 BINDING SITE, designated SEQ ID:34366, to the nucleotide sequence of VGAM1049 RNA, herein designated VGAM RNA, also designated SEQ ID:3760.

[38529] Another function of VGAM1049 is therefore inhibition of Placenta-specific 3 (PLAC3, Accession XM_045115). Accordingly, utilities of VGAM1049 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1050 (VGAM1050) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38530] VGAM1050 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1050 was detected is described hereinabove with reference to Figs. 1–8.

[38531] VGAM1050 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38532] VGAM1050 gene encodes a VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1050 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1050 precursor RNA is designated SEQ ID:1036, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1036 is located at position 108185 relative to the genome of Meleagrid Herpesvirus 1.

[38533] VGAM1050 precursor RNA folds onto itself, forming VGAM1050 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38534] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1050 folded precursor RNA into VGAM1050 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1050 RNA is designated SEQ ID:3761, and is provided hereinbelow with reference to the sequence listing part.

[38535] VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1050 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38536] VGAM1050 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1050 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1050 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38537] The complementary binding of VGAM1050 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1050 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1050 host target RNA into VGAM1050 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38538] It is appreciated that VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1050 host target genes. The mRNA of each one of this plurality of VGAM1050 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1050 RNA, herein designated VGAM RNA, and which when bound by VGAM1050 RNA causes inhibition of translation of respective one or more VGAM1050 host target proteins.

[38539] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1050 gene, herein designated VGAM GENE, on one or more VGAM1050 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38540] It is yet further appreciated that a function of VGAM1050 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1050 correlate with, and may be deduced from, the identity of the host target genes which VGAM1050 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38541] Nucleotide sequences of the VGAM1050 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1050 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1050 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1050 are further described hereinbelow with reference to Table 1.

[38542] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1050 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1050 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38543] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1050 gene, herein designated VGAM is inhibition of expression of VGAM1050 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1050 correlate with, and may be deduced from, the identity of the target genes which VGAM1050 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38544] ADP-ribosylation Factor-like 4 (ARL4, Accession NM_005738) is a VGAM1050 host target gene. ARL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARL4, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL4 BINDING SITE, designated SEQ ID:12298, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38545] A function of VGAM1050 is therefore inhibition of ADP-ribosylation Factor-like 4 (ARL4, Accession NM_005738), a gene which may be required for the progression of cells through meiosis. Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL4. The function of ARL4 has been established by previous studies. Schurmann et al. (1994) identified mouse *Arl4* as a gene that is abundantly expressed in differentiated cells of the preadipocyte cell line 3T3-L1 but is not detectably expressed in undifferentiated 3T3-L1 cells. By Northern blot analysis, Jacobs et al. (1998) found that rat *Arl4* is expressed predominantly in testis, at lower levels in spleen and intestine, and at even lower levels in brain, heart, total fat, liver, lung, and thymus. In situ hybridization of rat testis showed that *Arl4* is expressed in germ cells of puberal and adult testis, but not in prepuberal testis. Jacobs

et al. (1998) suggested that Arl4 is involved in sperm production. Animal model experiments lend further support to the function of ARL4. Schurmann et al. (2002) generated mice lacking Arl4. These mice did not have upregulated expression of other Arl genes in testis, were viable, and were apparently normal except for reduced testicular weight and sperm count. However, the remaining sperm had normal motility, and Arl4 $-/-$ mice were fertile and sired normal-size litters. Schurmann et al. (2002) proposed that ARL4 is required for the progression of cells through meiosis and that its deletion causes a retardation of the formation of haploid spermatides

[38546] It is appreciated that the abovementioned animal model for ARL4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[38547] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38548] Schurmann, A.; Breiner, M.; Becker, W.; Huppertz, C.; Kainulainen, H.; Kentrup, H.; Joost, H.-G. : Cloning of two novel ADP-ribosylation factor-like proteins and characterization of their differential expression in 3T3-L1 cells. J.

Biol. Chem. 269: 15683–15688, 1994. ; and

[38549] Schurmann, A.; Koling, S.; Jacobs, S.; Saftig, P.; Kraub, S.; Wennemuth, G.; Kluge, R.; Joost, H.–G. : Reduced sperm count and normal fertility in male mice with targeted disruption of.

[38550] Further studies establishing the function and utilities of ARL4 are found in John Hopkins OMIM database record ID 604786, and in cited publications numbered 665 and 7445–2905 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. GEMIN5 (Accession XM_114471) is another VGAM1050 host target gene. GEMIN5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GEMIN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GEMIN5 BINDING SITE, designated SEQ ID:42971, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38551] Another function of VGAM1050 is therefore inhibition of GEMIN5 (Accession XM_114471). Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GEMIN5. MAP-kinase Activating Death Domain (MADD, Accession NM_130476) is another VGAM1050 host target gene. MADD BINDING SITE1 through MADD BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MADD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADD BINDING SITE1 through MADD BINDING SITE6, designated SEQ ID:28254, SEQ ID:28239, SEQ ID:28233, SEQ ID:9784, SEQ ID:28249 and SEQ ID:28244 respectively, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38552] Another function of VGAM1050 is therefore inhibition of MAP-kinase Activating Death Domain (MADD, Accession NM_130476), a gene which may regulate two different pathways for neural activities.interacts with the type-1 tumor necrosis factor receptor (TNFR1); death domain-containing protein. Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADD. The function of MADD and its association with various diseases and clini-

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM_003615) is another VGAM1050 host target gene. SLC4A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A7 BINDING SITE, designated SEQ ID:9666, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38553] Another function of VGAM1050 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM_003615), a gene which mediates the coupled movement of sodium and bicarbonate ions across the plasma membrane. Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A7. The function of SLC4A7 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM66. Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837) is another VGAM1050 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16853, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38554] Another function of VGAM1050 is therefore inhibition of Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837). Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. LOC113612 (Accession XM_054492) is another VGAM1050 host target gene. LOC113612 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC113612 BINDING SITE, designated SEQ ID:36171, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38555] Another function of VGAM1050 is therefore inhibition of LOC113612 (Accession XM_054492). Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113612. LOC199920 (Accession XM_114056) is another VGAM1050 host target gene. LOC199920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199920 BINDING SITE, designated SEQ ID:42659, to the nucleotide sequence of VGAM1050 RNA, herein designated VGAM RNA, also designated SEQ ID:3761.

[38556] Another function of VGAM1050 is therefore inhibition of LOC199920 (Accession XM_114056). Accordingly, utilities of VGAM1050 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199920. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1051 (VGAM1051) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38557] VGAM1051 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1051 was detected is described hereinabove with reference to Figs. 1–8.

[38558] VGAM1051 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38559] VGAM1051 gene encodes a VGAM1051 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1051 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1051 precursor RNA is designated SEQ ID:1037, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1037 is located at position 110396 relative to the genome of Meleagrid Herpesvirus 1.

[38560] VGAM1051 precursor RNA folds onto itself, forming VGAM1051 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38561] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1051 folded precursor RNA into VGAM1051 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1051 RNA is designated SEQ ID:3762, and is provided hereinbelow with reference to the sequence listing part.

[38562] VGAM1051 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1051 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38563] VGAM1051 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1051 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1051 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1051 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[38564] The complementary binding of VGAM1051 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1051 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1051 host target RNA into VGAM1051 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38565] It is appreciated that VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1051 host target genes. The mRNA of each one of this plurality of VGAM1051 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1051 RNA, herein designated VGAM RNA, and which when bound by VGAM1051 RNA causes inhibition of translation of respective one or more

VGAM1051 host target proteins.

[38566] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1051 gene, herein designated VGAM GENE, on one or more VGAM1051 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38567] It is yet further appreciated that a function of VGAM1051 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1051 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1.

Specific functions, and accordingly utilities, of VGAM1051 correlate with, and may be deduced from, the identity of the host target genes which VGAM1051 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38568] Nucleotide sequences of the VGAM1051 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1051 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1051 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1051 are further described hereinbelow with reference to Table 1.

[38569] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1051 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1051 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38570] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1051 gene, herein designated VGAM is inhibition of expression of VGAM1051 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1051 correlate with, and may be deduced from, the identity of the target genes which VGAM1051 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38571] Flavin Containing Monooxygenase 5 (FMO5, Accession NM_001461) is a VGAM1051 host target gene. FMO5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMO5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMO5 BINDING SITE, designated SEQ ID:7193, to the nucleotide sequence of VGAM1051 RNA, herein designated VGAM RNA, also designated SEQ ID:3762.

[38572] A function of VGAM1051 is therefore inhibition of Flavin Containing Monooxygenase 5 (FMO5, Accession NM_001461), a gene which Flavin-containing monooxygenase 5; may catalyze the monooxygenation of xenobiotic soft nucleophiles. Accordingly, utilities of VGAM1051 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMO5. The function of FMO5 has been established by previous studies. The flavin-containing monooxygenases (FMOs; EC

1.14.13.8) catalyze the oxidation of nucleophilic nitrogen, sulfur, and phosphorus atoms in a wide variety of compounds, including many pesticides and drugs. See FMO1 (OMIM Ref. No. 136130). By screening liver libraries with a rabbit FMO5 cDNA, Overby et al. (1995) isolated cDNAs encoding guinea pig and human FMO5. The predicted 533-amino acid human protein shares 85% and 87% identity with rabbit and guinea pig FMO5, respectively. Northern blot analysis revealed that the human FMO5 gene was expressed as 2.6- and 3.8-kb mRNAs in liver. The FMO5 protein had an apparent molecular mass of 60 kD on Western blots of adult and neonatal human liver. All 3 mammalian FMO5 enzymes exhibited similar catalytic activities, which were distinct from those of other FMOs. The authors concluded that FMO5 is not an efficient drug-metabolizing enzyme and that it may have an alternative physiologic role. By PCR analysis of somatic cell hybrids, McCombie et al. (1996) mapped the FMO2 (OMIM Ref. No. 603955) and FMO5 genes to chromosome 1q, where 3 other human FMO genes are located. Using sequence analysis of a YAC contig, Gelb et al. (1997) found that the FMO5 gene is located between the NPR1 (OMIM Ref. No. 108960) and CX40 (GJA5; 121013) genes. By FISH, they

mapped this contig to 1q21.1. Gelb et al. (1997) noted that since the FMO1 gene maps to 1q23–q25, this excluded the possibility that a single gene cluster contains the entire FMO family.

[38573] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38574] McCombie, R. R.; Dolphin, C. T.; Povey, S.; Phillips, I. R.; Shephard, E. A. : Localization of human flavin-containing monooxygenase genes FMO2 and FMO5 to chromosome 1q. *Genomics* 34: 426–429, 1996. ; and

[38575] Overby, L. H.; Buckpitt, A. R.; Lawton, M. P.; Atta-Asafo-Adjei, E.; Schulze, J.; Philpot, R. M. : Characterization of flavin-containing monooxygenase 5 (FMO5) cloned from human and gui.

[38576] Further studies establishing the function and utilities of FMO5 are found in John Hopkins OMIM database record ID 603957, and in cited publications numbered 528 and 5285 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite Motif-containing 6 (TRIM6, Accession NM_058166) is another VGAM1051 host target gene. TRIM6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by TRIM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM6 BINDING SITE, designated SEQ ID:27713, to the nucleotide sequence of VGAM1051 RNA, herein designated VGAM RNA, also designated SEQ ID:3762.

[38577] Another function of VGAM1051 is therefore inhibition of Tripartite Motif-containing 6 (TRIM6, Accession NM_058166). Accordingly, utilities of VGAM1051 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM6. LOC152059 (Accession XM_087372) is another VGAM1051 host target gene. LOC152059 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152059 BINDING SITE, designated SEQ ID:39209, to the nucleotide sequence of VGAM1051 RNA, herein designated VGAM RNA, also designated SEQ ID:3762.

[38578] Another function of VGAM1051 is therefore inhibition of

LOC152059 (Accession XM_087372). Accordingly, utilities of VGAM1051 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152059. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1052 (VGAM1052) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38579] VGAM1052 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1052 was detected is described hereinabove with reference to Figs. 1-8.

[38580] VGAM1052 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38581] VGAM1052 gene encodes a VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1052 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1052 precursor RNA is designated SEQ ID:1038, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1038 is located at position 106911 relative to the genome of Meleagrid Herpesvirus 1.

- [38582] VGAM1052 precursor RNA folds onto itself, forming VGAM1052 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38583] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1052 folded precursor RNA into VGAM1052 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide se-

quence of VGAM1052 RNA is designated SEQ ID:3763, and is provided hereinbelow with reference to the sequence listing part.

[38584] VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1052 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38585] VGAM1052 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1052 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1052 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38586] The complementary binding of VGAM1052 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1052 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1052 host target RNA into VGAM1052 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38587] It is appreciated that VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1052 host target genes. The mRNA of each one of this plurality of VGAM1052 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1052 RNA, herein designated VGAM RNA, and which when bound by VGAM1052 RNA causes inhibition of translation of respective one or more VGAM1052 host target proteins.

[38588] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1052 gene, herein designated VGAM GENE, on one or more VGAM1052 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38589] It is yet further appreciated that a function of VGAM1052

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1052 correlate with, and may be deduced from, the identity of the host target genes which VGAM1052 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38590] Nucleotide sequences of the VGAM1052 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1052 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1052 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1052 are further described hereinbelow with reference to Table 1.

[38591] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1052 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1052 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38592] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1052 gene, herein designated VGAM is inhibition of expression of VGAM1052 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1052 correlate with, and may be deduced from, the identity of the target genes which VGAM1052 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38593] Bromodomain and PHD Finger Containing, 1 (BRPF1, Accession XM_054520) is a VGAM1052 host target gene. BRPF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRPF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRPF1 BINDING SITE, designated SEQ ID:36172, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38594] A function of VGAM1052 is therefore inhibition of Bromodomain and PHD Finger Containing, 1 (BRPF1, Accession XM_054520), a gene which has 6 zinc finger motifs and a bromodomain. Accordingly, utilities of VGAM1052

include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRPF1. The function of BRPF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497. Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033355) is another VGAM1052 host target gene. CASP8 BINDING SITE1 and CASP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP8 BINDING SITE1 and CASP8 BINDING SITE2, designated SEQ ID:27202 and SEQ ID:27206 respectively, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38595] Another function of VGAM1052 is therefore inhibition of Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033355), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM1052 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM145. DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366) is another VGAM1052 host target gene. DFFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DFFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DFFB BINDING SITE, designated SEQ ID:42240, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38596] Another function of VGAM1052 is therefore inhibition of DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366), a gene which induces DNA fragmentation and chromatin condensation during apoptosis. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DFFB.

The function of DFFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Thyroid Autoantigen 70kDa (Ku antigen) (G22P1, Accession NM_001469) is another VGAM1052 host target gene. G22P1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by G22P1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G22P1 BINDING SITE, designated SEQ ID:7202, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38597] Another function of VGAM1052 is therefore inhibition of Thyroid Autoantigen 70kDa (Ku antigen) (G22P1, Accession NM_001469), a gene which has a role in chromosome translocation. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G22P1. The function of G22P1 has been established by previous studies. The G22P1 gene encodes subunit p70 of the p70/p80 autoantigen. The p70/p80 autoantigen consists of 2 pro-

teins of molecular mass of approximately 70,000 and 80,000 daltons that dimerize to form a 10 S DNA-binding complex. See 194364 for discussion of the gene encoding the p80 subunit. Exchange of immunologic reagents showed that the p70/p80 autoantigen is identical to the Ku antigen, the Ki antigen, and the 86- to 70-kD protein complex. The p70/p80 complex binds to the ends of double-stranded DNA in a cell cycle-dependent manner, being associated with chromosomes of interphase cells, followed by complete dissociation from the condensing chromosomes in early prophase. Both p70 and p80 contain phosphoserine residues. A role for the antigen in DNA repair or transposition has been proposed. Animal model experiments lend further support to the function of G22P1. Li et al. (1998) presented evidence that inactivation of the Ku70 gene by targeted disruption in mice and derived cell lines leads to a propensity for malignant transformation both in vitro and in vivo. In vitro, Ku70 $-/-$ mouse fibroblasts displayed an increased rate of sister chromatid exchange and a high frequency of spontaneous neoplastic transformation. In vivo, Ku70 $-/-$ mice, known to be defective in B- but not T-lymphocyte maturation, developed thymic and disseminated T-cell lymphomas at

a mean age of 6 months with CD4+ /CD8+ tumor cells. In addition, many of the knockout mice showed segmental aganglionosis affecting the small intestine and the colon. These findings demonstrated that Ku70 deficiency facilitates neoplastic growth and suggested a role of the Ku70 locus in tumor suppression.

[38598] It is appreciated that the abovementioned animal model for G22P1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[38599] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38600] Li, G. C.; Ouyang, H.; Li, X.; Nagasawa, H.; Little, J. B.; Chen, D. J.; Ling, C. C.; Fuks, Z.; Cordon-Cardo, C. : Ku70: a candidate tumor suppressor gene for murine T cell lymphoma. *Molec. Cell* 2: 1-8, 1998. ; and

[38601] Reeves, W. H.; Sthoeger, Z. M. : Molecular cloning of cDNA encoding the p70 (Ku) lupus autoantigen. *J. Biol. Chem.* 264: 5047-5052, 1989.

[38602] Further studies establishing the function and utilities of G22P1 are found in John Hopkins OMIM database record ID 152690, and in cited publications numbered 88 and

1828–1840 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 4 (GRM4, Accession NM_000841) is another VGAM1052 host target gene. GRM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM4 BINDING SITE, designated SEQ ID:6503, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38603] Another function of VGAM1052 is therefore inhibition of Glutamate Receptor, Metabotropic 4 (GRM4, Accession NM_000841), a gene which is mediated by a g-protein that inhibits adenylate cyclase activity. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM4. The function of GRM4 has been established by previous studies. L-glutamate is the major excitatory neurotransmitter in the central nervous system and activates both ionotropic and metabotropic glutamate receptors. See mGluR3 (OMIM Ref. No. 601115). The metabotropic

glutamate receptors (OMIM Ref. No. mGluRs), which are G protein-coupled receptors, have been divided into 3 groups on the basis of sequence homology, putative signal transduction mechanisms, and pharmacologic properties. Group II and group III mGluRs are linked to the inhibition of the cyclic AMP cascade, but differ in their agonist selectivities. Group III agonists include L-2-amino-4-phosphonobutyrate (L-AP4) and L-serine-O-phosphate (Wu et al., 1998). Animal model experiments lend further support to the function of GRM4. To provide a better understanding of the L-AP4 receptors, Pekhletski et al. (1996) generated knockout mice lacking the mGluR4 gene. The mutant mice did not display any gross motor abnormalities, impairments of novelty-induced exploratory behaviors, or alterations in fine motor coordination. However, they were deficient on the rotating rod motor-learning test, suggesting that they may have an impaired ability to learn complex motor tasks. Analysis of presynaptic short-term synaptic plasticity at the parallel fiber-Purkinje cell synapse demonstrated that paired-pulse facilitation and post-tetanic potentiation were impaired in the mutant mice, although long-term depression was unaffected. Pekhletski et al. (1996) concluded that an

important function of mGluR4 is to provide a presynaptic mechanism for maintaining synaptic efficacy during repetitive activation, and that the presence of mGluR4 at the parallel fiber–Purkinje cell synapse is required for maintaining normal motor function. Gerlai et al. (1998) found that mGluR4 mutant mice exhibited significantly accelerated learning performance in a spatial reversal learning task. In a probe trial administered 6 weeks post-training, the mice showed impaired spatial accuracy. These results suggested that mGluR4 mutant mice differ in their ability to learn and integrate new spatial information into previously formed memory traces and that their use of stored spatial information is altered.

[38604] It is appreciated that the abovementioned animal model for GRM4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[38605] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38606] Pekhletski, R.; Gerlai, R.; Overstreet, L. S.; Huang, X. P.; Agopyan, N.; Slater, N. T.; Abramow–Newerly, W.; Roder, J. C.; Hampson, D. R. : Impaired cerebellar synaptic plasticity

and motor performance in mice lacking the mGluR4 subtype of metabotropic glutamate receptor. J. Neurosci. 16: 6364–6373, 1996. ; and

[38607] Wu, S.; Wright, R. A.; Rockey, P. K.; Burgett, S. G.; Arnold, J. S.; Rosteck, P. R., Jr.; Johnson, B. G.; Schoepp, D. D.; Belagaje, R. M. : Group III human metabotropic glutamate recepto.

[38608] Further studies establishing the function and utilities of GRM4 are found in John Hopkins OMIM database record ID 604100, and in cited publications numbered 5436, 5844–504 and 6361 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM_000868) is another VGAM1052 host target gene. HTR2C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTR2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR2C BINDING SITE, designated SEQ ID:6533, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38609] Another function of VGAM1052 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 2C (HTR2C, Accession NM_000868), a gene which activates phospholipase C and regulates intracellular calcium flux. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR2C. The function of HTR2C has been established by previous studies. Hall (1947) found that DBA/2 mice exhibited genetic susceptibility to audiogenic seizures (AGSs) stimulated by a doorbell mounted in an iron tub. Thereafter, audiogenic seizures were among the intensively studied phenotypes in behavioral genetics. Brennan et al. (1997) found that null mutant mice lacking serotonin 5-HT_{2C} receptors are extremely susceptible to AGSs. The onset of susceptibility was between 2 and 3 months of age, with complete penetrance in adult animals. Heisler et al. (2002) hypothesized that 5-HT receptors are expressed in POMC (OMIM Ref. No. 176830) neurons and that action at these receptors mediates a component of the anorexic effect of d-FEN (D-fenfluramine). Heisler et al. (2002) found that up to 80% of alpha-MSH neurons express HTR2C mRNA and that the pattern of co-expression was greatest in the caudal arcuate nucleus of

the hypothalamus. Heisler et al. (2002) demonstrated that direct activation of HTR2C by agonist in rats decreased their food intake and showed increased induction of FOS-like immunoreactivity in a pattern persistent with d-FEN-induced FOS-like immunoreactivity expression in the arcuate nucleus and paraventricular nucleus of the hypothalamus. Heisler et al. (2002) demonstrated that d-FEN directly activates POMC neurons, indicating that central 5-HT systems directly activate POMC neurons.

[38610] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38611] Heisler, L. K.; Cowley, M. A.; Tecott, L. H.; Fan, W.; Low, M. J.; Smart, J. L.; Rubinstein, M.; Tatro, J. B.; Marcus, J. N.; Holstege, H.; Lee, C. E.; Cone, R. D.; Elmquist, J. K. : Activation of central melanocortin pathways by fenfluramine. *Science* 297: 609–611, 2002. ; and

[38612] Tecott, L. H.; Sun, L. M.; Akana, S. F.; Strack, A. M.; Lowenstein, D. H.; Dallman, M. F.; Julius, D. : Eating disorder and epilepsy in mice lacking 5-HT_{2C} serotonin receptors. *Nature* 3.

[38613] Further studies establishing the function and utilities of HTR2C are found in John Hopkins OMIM database record

ID 312861, and in cited publications numbered 10618–1062 and 11464–10623 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kelch-like 1 (Drosophila) (KLHL1, Accession NM_020866) is another VGAM1052 host target gene. KLHL1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KLHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL1 BINDING SITE, designated SEQ ID:21918, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38614] Another function of VGAM1052 is therefore inhibition of Kelch-like 1 (Drosophila) (KLHL1, Accession NM_020866). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL1. LIM Homeobox Protein 2 (LHX2, Accession NM_004789) is another VGAM1052 host target gene. LHX2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LHX2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHX2 BINDING SITE, designated SEQ ID:11199, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38615] Another function of VGAM1052 is therefore inhibition of LIM Homeobox Protein 2 (LHX2, Accession NM_004789). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHX2. NIMA (never in mitosis gene a)-related Kinase 4 (NEK4, Accession NM_003157) is another VGAM1052 host target gene. NEK4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NEK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEK4 BINDING SITE, designated SEQ ID:9137, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38616] Another function of VGAM1052 is therefore inhibition of NIMA (never in mitosis gene a)-related Kinase 4 (NEK4,

Accession NM_003157). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEK4. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM1052 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE, designated SEQ ID:11062, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38617] Another function of VGAM1052 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. ADP-ribosylation Factor GT-

Pase Activating Protein 1 (ARFGAP1, Accession NM_018209) is another VGAM1052 host target gene. ARFGAP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARFGAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARFGAP1 BINDING SITE, designated SEQ ID:20109, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38618] Another function of VGAM1052 is therefore inhibition of ADP-ribosylation Factor GTPase Activating Protein 1 (ARFGAP1, Accession NM_018209). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARFGAP1. Chromosome 20 Open Reading Frame 124 (C20orf124, Accession NM_024777) is another VGAM1052 host target gene. C20orf124 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf124, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of C20orf124 BINDING SITE, designated SEQ ID:24144, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38619] Another function of VGAM1052 is therefore inhibition of Chromosome 20 Open Reading Frame 124 (C20orf124, Accession NM_024777). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf124. CG012 (Accession XM_096710) is another VGAM1052 host target gene. CG012 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CG012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG012 BINDING SITE, designated SEQ ID:40486, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38620] Another function of VGAM1052 is therefore inhibition of CG012 (Accession XM_096710). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG012.

DJ667H12.2 (Accession NM_019605) is another VGAM1052 host target gene. DJ667H12.2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DJ667H12.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ667H12.2 BINDING SITE, designated SEQ ID:21215, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38621] Another function of VGAM1052 is therefore inhibition of DJ667H12.2 (Accession NM_019605). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ667H12.2. Dystrophia Myotonica-containing WD Repeat Motif (DMWD, Accession XM_027569) is another VGAM1052 host target gene. DMWD BINDING SITE1 and DMWD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMWD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMWD BINDING SITE1 and DMWD BINDING

SITE2, designated SEQ ID:30528 and SEQ ID:30530 respectively, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38622] Another function of VGAM1052 is therefore inhibition of Dystrophia Myotonica-containing WD Repeat Motif (DMWD, Accession XM_027569). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMWD. FLJ10661 (Accession NM_018172) is another VGAM1052 host target gene. FLJ10661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10661 BINDING SITE, designated SEQ ID:19994, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38623] Another function of VGAM1052 is therefore inhibition of FLJ10661 (Accession NM_018172). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10661. FLJ12650 (Accession NM_024522) is another VGAM1052 host target gene. FLJ12650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12650 BINDING SITE, designated SEQ ID:23722, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38624] Another function of VGAM1052 is therefore inhibition of FLJ12650 (Accession NM_024522). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12650. KIAA0356 (Accession XM_038655) is another VGAM1052 host target gene. KIAA0356 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0356, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0356 BINDING SITE, designated SEQ ID:32891, to the nucleotide sequence of VGAM1052 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3763.

[38625] Another function of VGAM1052 is therefore inhibition of KIAA0356 (Accession XM_038655). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0356. KIAA1464 (Accession XM_043069) is another VGAM1052 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33881, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38626] Another function of VGAM1052 is therefore inhibition of KIAA1464 (Accession XM_043069). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1464. PRO0365 (Accession NM_014126) is another VGAM1052 host target gene. PRO0365 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0365, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0365 BINDING SITE, designated SEQ ID:15388, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38627] Another function of VGAM1052 is therefore inhibition of PRO0365 (Accession NM_014126). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0365. SC65 (Accession NM_006455) is another VGAM1052 host target gene. SC65 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SC65, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SC65 BINDING SITE, designated SEQ ID:13174, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38628] Another function of VGAM1052 is therefore inhibition of SC65 (Accession NM_006455). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SC65. Septin 3 (SEPT3, Accession NM_019106) is another VGAM1052 host target gene. SEPT3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SEPT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT3 BINDING SITE, designated SEQ ID:21179, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38629] Another function of VGAM1052 is therefore inhibition of Septin 3 (SEPT3, Accession NM_019106). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPT3. TED (Accession NM_015686) is another VGAM1052 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17914, to the nucleotide sequence of

VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38630] Another function of VGAM1052 is therefore inhibition of TED (Accession NM_015686). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. LOC129195 (Accession XM_066378) is another VGAM1052 host target gene. LOC129195 BINDING SITE1 through LOC129195 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC129195, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129195 BINDING SITE1 through LOC129195 BINDING SITE3, designated SEQ ID:37323, SEQ ID:37324 and SEQ ID:37325 respectively, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38631] Another function of VGAM1052 is therefore inhibition of LOC129195 (Accession XM_066378). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129195. LOC149606 (Accession XM_086600) is an-

other VGAM1052 host target gene. LOC149606 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149606, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149606 BINDING SITE, designated SEQ ID:38782, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38632] Another function of VGAM1052 is therefore inhibition of LOC149606 (Accession XM_086600). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149606. LOC150197 (Accession XM_086801) is another VGAM1052 host target gene. LOC150197 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150197 BINDING SITE, designated SEQ ID:38866, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38633] Another function of VGAM1052 is therefore inhibition of LOC150197 (Accession XM_086801). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150197. LOC158490 (Accession XM_088585) is another VGAM1052 host target gene. LOC158490 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158490 BINDING SITE, designated SEQ ID:39848, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38634] Another function of VGAM1052 is therefore inhibition of LOC158490 (Accession XM_088585). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158490. LOC220073 (Accession XM_167847) is another VGAM1052 host target gene. LOC220073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220073, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220073 BINDING SITE, designated SEQ ID:44874, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38635] Another function of VGAM1052 is therefore inhibition of LOC220073 (Accession XM_167847). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220073. LOC90917 (Accession XM_034861) is another VGAM1052 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32164, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38636] Another function of VGAM1052 is therefore inhibition of LOC90917 (Accession XM_034861). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90917. LOC91069 (Accession XM_035824) is another VGAM1052 host target gene. LOC91069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91069 BINDING SITE, designated SEQ ID:32346, to the nucleotide sequence of VGAM1052 RNA, herein designated VGAM RNA, also designated SEQ ID:3763.

[38637] Another function of VGAM1052 is therefore inhibition of LOC91069 (Accession XM_035824). Accordingly, utilities of VGAM1052 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91069. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1053 (VGAM1053) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38638] VGAM1053 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1053 was detected is described hereinabove with reference to Figs. 1–8.

[38639] VGAM1053 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38640] VGAM1053 gene encodes a VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1053 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1053 precursor RNA is designated SEQ ID:1039, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1039 is located at position 104991 relative to the genome of Meleagrid Herpesvirus 1.

[38641] VGAM1053 precursor RNA folds onto itself, forming VGAM1053 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38642] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1053 folded precursor RNA into VGAM1053 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1053 RNA is designated SEQ ID:3764, and is provided hereinbelow with reference to the sequence listing part.

[38643] VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1053 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38644] VGAM1053 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1053 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1053 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[38645] The complementary binding of VGAM1053 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1053 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1053 host target RNA into VGAM1053 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38646] It is appreciated that VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1053 host target genes. The mRNA of each one of this plurality of VGAM1053 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1053 RNA, herein designated VGAM RNA, and which when bound by VGAM1053 RNA causes inhibition of translation of respective one or more VGAM1053 host target proteins.

[38647] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1053 gene, herein designated VGAM GENE, on one or more VGAM1053 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38648] It is yet further appreciated that a function of VGAM1053 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1053 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1053 correlate with, and may be deduced from, the identity of the host target genes which VGAM1053 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38649] Nucleotide sequences of the VGAM1053 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1053 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1053 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1053 are further described hereinbelow with reference to Table 1.

[38650] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1053 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1053 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38651] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1053 gene, herein designated VGAM is inhibition of expression of VGAM1053 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1053 correlate with, and may be deduced from, the identity of the target genes which VGAM1053 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38652] Oncostatin M Receptor (OSMR, Accession NM_003999) is a VGAM1053 host target gene. OSMR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OSMR, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSMR BINDING SITE, designated SEQ ID:10150, to the nucleotide sequence of VGAM1053 RNA, herein designated VGAM RNA, also designated SEQ ID:3764.

[38653] A function of VGAM1053 is therefore inhibition of Oncostatin M Receptor (OSMR, Accession NM_003999). Accordingly, utilities of VGAM1053 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSMR. LOC127943 (Accession XM_059195) is another VGAM1053 host target gene. LOC127943 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127943 BINDING SITE, designated SEQ ID:36913, to the nucleotide sequence of VGAM1053 RNA, herein designated VGAM RNA, also designated SEQ ID:3764.

[38654] Another function of VGAM1053 is therefore inhibition of LOC127943 (Accession XM_059195). Accordingly, utilities of VGAM1053 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC127943. LOC131873 (Accession XM_067585) is another VGAM1053 host target gene. LOC131873 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131873 BINDING SITE, designated SEQ ID:37365, to the nucleotide sequence of VGAM1053 RNA, herein designated VGAM RNA, also designated SEQ ID:3764.

[38655] Another function of VGAM1053 is therefore inhibition of LOC131873 (Accession XM_067585). Accordingly, utilities of VGAM1053 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131873. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1054 (VGAM1054) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38656] VGAM1054 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1054 was detected is described hereinabove with reference to Figs. 1–8.

[38657] VGAM1054 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38658] VGAM1054 gene encodes a VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1054 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1054 precursor RNA is designated SEQ ID:1040, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1040 is located at position 193129 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[38659] VGAM1054 precursor RNA folds onto itself, forming VGAM1054 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38660] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1054 folded precursor RNA into VGAM1054 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1054 RNA is designated SEQ ID:3765, and is provided hereinbelow with reference to the sequence listing part.

[38661] VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1054 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38662] VGAM1054 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1054 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1054 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38663] The complementary binding of VGAM1054 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1054 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1054 host target RNA into VGAM1054 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38664] It is appreciated that VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1054 host target genes. The mRNA of each one of this plurality of VGAM1054 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1054 RNA, herein designated VGAM RNA, and which when bound by VGAM1054 RNA causes inhibition of translation of respective one or more VGAM1054 host target proteins.

[38665] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1054 gene, herein designated VGAM GENE, on one or more VGAM1054 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38666] It is yet further appreciated that a function of VGAM1054 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1054 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1054 correlate with, and may be deduced from, the identity of the host target genes which VGAM1054 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38667] Nucleotide sequences of the VGAM1054 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1054 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1054 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1054 are further described hereinbelow with reference to Table 1.

[38668] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1054 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1054 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38669] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1054 gene, herein designated VGAM is inhibition of expression of VGAM1054 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1054 correlate with, and may be deduced from, the identity of the target genes which VGAM1054 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38670] Ras Homolog Gene Family, Member E (ARHE, Accession NM_005168) is a VGAM1054 host target gene. ARHE BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by ARHE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHE BINDING SITE, designated SEQ ID:11670, to the nucleotide sequence of VGAM1054 RNA, herein designated VGAM RNA, also designated SEQ ID:3765.

[38671] A function of VGAM1054 is therefore inhibition of Ras Homolog Gene Family, Member E (ARHE, Accession NM_005168). Accordingly, utilities of VGAM1054 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHE. FLJ11116 (Accession XM_093216) is another VGAM1054 host target gene. FLJ11116 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11116 BINDING SITE, designated SEQ ID:40185, to the nucleotide sequence of VGAM1054 RNA, herein designated VGAM RNA, also designated SEQ ID:3765.

[38672] Another function of VGAM1054 is therefore inhibition of

FLJ11116 (Accession XM_093216). Accordingly, utilities of VGAM1054 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11116. KIAA1136 (Accession XM_166110) is another VGAM1054 host target gene. KIAA1136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1136 BINDING SITE, designated SEQ ID:43886, to the nucleotide sequence of VGAM1054 RNA, herein designated VGAM RNA, also designated SEQ ID:3765.

[38673] Another function of VGAM1054 is therefore inhibition of KIAA1136 (Accession XM_166110). Accordingly, utilities of VGAM1054 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1136. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1055 (VGAM1055) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[38674] VGAM1055 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1055 was detected is described hereinabove with reference to Figs. 1–8.

[38675] VGAM1055 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mayaro Virus. VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38676] VGAM1055 gene encodes a VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1055 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1055 precursor RNA is designated SEQ ID:1041, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1041 is located at position 10628 relative to the genome of Mayaro Virus.

[38677] VGAM1055 precursor RNA folds onto itself, forming VGAM1055 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38678] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1055 folded precursor RNA into VGAM1055 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1055 RNA is designated SEQ ID:3766, and is provided hereinbelow with reference to the sequence listing part.

[38679] VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1055 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[38680] VGAM1055 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1055 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1055 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[38681] The complementary binding of VGAM1055 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1055 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1055 host target RNA into VGAM1055 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38682] It is appreciated that VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1055 host target genes. The mRNA of each one of this plurality of VGAM1055 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1055 RNA, herein designated VGAM RNA, and which when bound by VGAM1055 RNA causes inhibition of translation of respective one or more VGAM1055 host target proteins.

[38683] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1055 gene, herein designated VGAM GENE, on one

or more VGAM1055 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38684] It is yet further appreciated that a function of VGAM1055 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment of viral infection by Mayaro Virus. Specific functions, and accordingly utilities, of VGAM1055 correlate with, and may be deduced from, the identity of the host target genes which VGAM1055 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38685] Nucleotide sequences of the VGAM1055 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1055 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1055 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1055 are further described hereinbelow with reference to Table 1.

[38686] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1055 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1055 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38687] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1055 gene, herein designated VGAM is inhibition of expression of VGAM1055 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1055 correlate with, and may be deduced from, the identity of the target genes which VGAM1055 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38688] ATPase, Class VI, Type 11B (ATP11B, Accession

XM_087254) is a VGAM1055 host target gene. ATP11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11B BINDING SITE, designated SEQ ID:39143, to the nucleotide sequence of VGAM1055 RNA, herein designated VGAM RNA, also designated SEQ ID:3766.

[38689] A function of VGAM1055 is therefore inhibition of ATPase, Class VI, Type 11B (ATP11B, Accession XM_087254), a gene which is phosphorylated in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11B. The function of ATP11B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM665.KIAA0442 (Accession NM_015570) is another VGAM1055 host target gene. KIAA0442 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0442, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0442 BINDING SITE, designated SEQ ID:17843, to the nucleotide sequence of VGAM1055 RNA, herein designated VGAM RNA, also designated SEQ ID:3766.

[38690] Another function of VGAM1055 is therefore inhibition of KIAA0442 (Accession NM_015570). Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0442. MIPOL1 (Accession XM_085077) is another VGAM1055 host target gene. MIPOL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MIPOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIPOL1 BINDING SITE, designated SEQ ID:37814, to the nucleotide sequence of VGAM1055 RNA, herein designated VGAM RNA, also designated SEQ ID:3766.

[38691] Another function of VGAM1055 is therefore inhibition of MIPOL1 (Accession XM_085077). Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MIPOL1. LOC256789 (Accession XM_173369) is another VGAM1055 host target gene. LOC256789 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256789 BINDING SITE, designated SEQ ID:46539, to the nucleotide sequence of VGAM1055 RNA, herein designated VGAM RNA, also designated SEQ ID:3766.

[38692] Another function of VGAM1055 is therefore inhibition of LOC256789 (Accession XM_173369). Accordingly, utilities of VGAM1055 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256789. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1056 (VGAM1056) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38693] VGAM1056 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1056 was detected is described hereinabove with reference to Figs. 1–8.

[38694] VGAM1056 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Mayaro Virus.

VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38695] VGAM1056 gene encodes a VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1056 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1056 precursor RNA is designated SEQ ID:1042, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1042 is located at position 10251 relative to the genome of Mayaro Virus.

[38696] VGAM1056 precursor RNA folds onto itself, forming VGAM1056 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38697] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1056 folded precursor RNA into VGAM1056 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1056 RNA is designated SEQ ID:3767, and is provided hereinbelow with reference to the sequence listing part.

[38698] VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1056 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38699] VGAM1056 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1056 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1056 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38700] The complementary binding of VGAM1056 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1056 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1056 host target RNA into VGAM1056 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38701] It is appreciated that VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1056 host target genes. The mRNA of each one of this plurality of VGAM1056 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1056 RNA, herein designated VGAM RNA, and which when bound by VGAM1056 RNA causes inhibition of translation of respective one or more VGAM1056 host target proteins.

[38702] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1056 gene, herein designated VGAM GENE, on one or more VGAM1056 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38703] It is yet further appreciated that a function of VGAM1056 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1056 include diagnosis, prevention and treatment of viral infection by Mayaro Virus. Specific functions, and accordingly utilities, of VGAM1056 correlate with, and may be deduced from, the identity of the host target genes which VGAM1056 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38704] Nucleotide sequences of the VGAM1056 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1056 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1056 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1056 are further described hereinbelow with reference to Table 1.

[38705] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1056 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1056 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38706] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1056 gene, herein designated VGAM is inhibition of expression of VGAM1056 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1056 correlate with, and may be deduced from, the identity of the target genes which VGAM1056 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38707] LOC148887 (Accession XM_097537) is a VGAM1056 host target gene. LOC148887 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by LOC148887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148887 BINDING SITE, designated SEQ ID:40911, to the nucleotide sequence of VGAM1056 RNA, herein designated VGAM RNA, also designated SEQ ID:3767.

[38708] A function of VGAM1056 is therefore inhibition of LOC148887 (Accession XM_097537). Accordingly, utilities of VGAM1056 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148887. LOC90632 (Accession XM_033067) is another VGAM1056 host target gene. LOC90632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90632 BINDING SITE, designated SEQ ID:31830, to the nucleotide sequence of VGAM1056 RNA, herein designated VGAM RNA, also designated SEQ ID:3767.

[38709] Another function of VGAM1056 is therefore inhibition of LOC90632 (Accession XM_033067). Accordingly, utilities

of VGAM1056 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90632. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1057 (VGAM1057) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38710] VGAM1057 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1057 was detected is described hereinabove with reference to Figs. 1-8.

[38711] VGAM1057 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid Herpesvirus 4. VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38712] VGAM1057 gene encodes a VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1057 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1057 precursor RNA is designated SEQ ID:1043, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1043 is located at position 101664 relative to the genome of Murid Herpesvirus 4.

- [38713] VGAM1057 precursor RNA folds onto itself, forming VGAM1057 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38714] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1057 folded precursor RNA into VGAM1057 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 86%) nucleotide sequence of VGAM1057 RNA is designated SEQ ID:3768, and

is provided hereinbelow with reference to the sequence listing part.

[38715] VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1057 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[38716] VGAM1057 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1057 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1057 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38717] The complementary binding of VGAM1057 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1057 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1057 host target RNA into VGAM1057 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38718] It is appreciated that VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1057 host target genes. The mRNA of each one of this plurality of VGAM1057 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1057 RNA, herein designated VGAM RNA, and which when bound by VGAM1057 RNA causes inhibition of translation of respective one or more VGAM1057 host target proteins.

[38719] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1057 gene, herein designated VGAM GENE, on one or more VGAM1057 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38720] It is yet further appreciated that a function of VGAM1057 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1057 include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1057 correlate with, and may be deduced from, the identity of the host target genes which VGAM1057 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38721] Nucleotide sequences of the VGAM1057 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1057 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1057 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1057 are further described hereinbelow with reference to Table 1.

[38722] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1057 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1057 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38723] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1057 gene, herein designated VGAM is inhibition of expression of VGAM1057 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1057 correlate with, and may be deduced from, the identity of the target genes which VGAM1057 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38724] Integrin, Beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12) (ITGB1, Accession NM_033666) is a VGAM1057 host target gene. ITGB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB1 BINDING SITE, designated SEQ ID:27394, to the nucleotide sequence of VGAM1057 RNA, herein designated VGAM RNA, also designated SEQ ID:3768.

[38725] A function of VGAM1057 is therefore inhibition of Integrin, Beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12) (ITGB1, Accession NM_033666), a gene which acts as a fibronectin receptor. Accordingly, utilities of VGAM1057 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with ITGB1. The function of ITGB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM427.KIAA0258 (Accession NM_014785) is another VGAM1057 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16650, to the nucleotide sequence of VGAM1057 RNA, herein designated VGAM RNA, also designated SEQ ID:3768.

[38726] Another function of VGAM1057 is therefore inhibition of KIAA0258 (Accession NM_014785). Accordingly, utilities of VGAM1057 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA1819 (Accession XM_045716) is another VGAM1057 host target gene. KIAA1819 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1819, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1819 BINDING SITE, designated SEQ ID:34535, to the nucleotide sequence of VGAM1057 RNA, herein designated VGAM RNA, also designated SEQ ID:3768.

[38727] Another function of VGAM1057 is therefore inhibition of KIAA1819 (Accession XM_045716). Accordingly, utilities of VGAM1057 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1819. LOC255862 (Accession XM_170505) is another VGAM1057 host target gene. LOC255862 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255862, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255862 BINDING SITE, designated SEQ ID:45340, to the nucleotide sequence of VGAM1057 RNA, herein designated VGAM RNA, also designated SEQ ID:3768.

[38728] Another function of VGAM1057 is therefore inhibition of LOC255862 (Accession XM_170505). Accordingly, utilities of VGAM1057 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC255862. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1058 (VGAM1058) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38729] VGAM1058 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1058 was detected is described hereinabove with reference to Figs. 1–8.

[38730] VGAM1058 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid Herpesvirus 4. VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38731] VGAM1058 gene encodes a VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1058 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1058 precursor RNA is desig-

nated SEQ ID:1044, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1044 is located at position 98739 relative to the genome of Murid Herpesvirus 4.

- [38732] VGAM1058 precursor RNA folds onto itself, forming VGAM1058 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [38733] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1058 folded precursor RNA into VGAM1058 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1058 RNA is designated SEQ ID:3769, and is provided hereinbelow with reference to the sequence

listing part.

[38734] VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1058 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38735] VGAM1058 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1058 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1058 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38736] The complementary binding of VGAM1058 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1058 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1058 host target RNA into VGAM1058 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38737] It is appreciated that VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1058 host target genes. The mRNA of each one of this plurality of VGAM1058 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1058 RNA, herein designated VGAM

RNA, and which when bound by VGAM1058 RNA causes inhibition of translation of respective one or more VGAM1058 host target proteins.

[38738] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1058 gene, herein designated VGAM GENE, on one or more VGAM1058 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38739] It is yet further appreciated that a function of VGAM1058 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1058

correlate with, and may be deduced from, the identity of the host target genes which VGAM1058 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38740] Nucleotide sequences of the VGAM1058 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1058 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1058 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1058 are further described hereinbelow with reference to Table 1.

[38741] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1058 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1058 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38742] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1058 gene, herein designated VGAM is inhibition of expression of VGAM1058 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1058 correlate with, and may be deduced

from, the identity of the target genes which VGAM1058 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38743] Absent In Melanoma 1 (AIM1, Accession XM_166300) is a VGAM1058 host target gene. AIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AIM1 BINDING SITE, designated SEQ ID:44116, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38744] A function of VGAM1058 is therefore inhibition of Absent In Melanoma 1 (AIM1, Accession XM_166300), a gene which interactions with the cytoskeleton. Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AIM1. The function of AIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM808. Aspartate Beta-hydroxylase (ASPH, Accession NM_032466) is another VGAM1058 host target

gene. ASPH BINDING SITE1 and ASPH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ASPH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASPH BINDING SITE1 and ASPH BINDING SITE2, designated SEQ ID:26221 and SEQ ID:26226 respectively, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38745] Another function of VGAM1058 is therefore inhibition of Aspartate Beta-hydroxylase (ASPH, Accession NM_032466), a gene which specifically hydroxylates the beta carbon of aspartic acid or asparagine residues in certain epidermal growth factor (EGF)-like domains of a number of proteins. Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASPH. The function of ASPH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM47.Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540) is another VGAM1058

host target gene. MAT1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAT1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT1A BINDING SITE, designated SEQ ID:43669, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38746] Another function of VGAM1058 is therefore inhibition of Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT1A. Neuroblastoma RAS Viral (v-ras) Oncogene Homolog (NRAS, Accession NM_002524) is another VGAM1058 host target gene. NRAS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NRAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRAS BINDING SITE, designated SEQ ID:8363, to the nucleotide sequence of VGAM1058 RNA, herein

designated VGAM RNA, also designated SEQ ID:3769.

[38747] Another function of VGAM1058 is therefore inhibition of Neuroblastoma RAS Viral (v-ras) Oncogene Homolog (NRAS, Accession NM_002524), a gene which ras proteins bind gdp/gtp and possess intrinsic gtpase activity. Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRAS. The function of NRAS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM351.3-oxoacid CoA Transferase (OXCT, Accession NM_000436) is another VGAM1058 host target gene. OXCT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OXCT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OXCT BINDING SITE, designated SEQ ID:6019, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38748] Another function of VGAM1058 is therefore inhibition of 3-oxoacid CoA Transferase (OXCT, Accession

NM_000436). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OXCT. Calcium-binding tyrosine-(Y)-phosphorylation Regulated (fibrousheathin 2) (CABYR, Accession NM_012189) is another VGAM1058 host target gene. CABYR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CABYR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CABYR BINDING SITE, designated SEQ ID:14478, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38749] Another function of VGAM1058 is therefore inhibition of Calcium-binding tyrosine-(Y)-phosphorylation Regulated (fibrousheathin 2) (CABYR, Accession NM_012189). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CABYR. DKFZp434K1210 (Accession NM_017606) is another VGAM1058 host target gene. DKFZp434K1210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DKFZp434K1210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434K1210 BINDING SITE, designated SEQ ID:19101, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38750] Another function of VGAM1058 is therefore inhibition of DKFZp434K1210 (Accession NM_017606). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434K1210. DKFZP566D1346 (Accession NM_030816) is another VGAM1058 host target gene. DKFZP566D1346 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566D1346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566D1346 BINDING SITE, designated SEQ ID:25137, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38751] Another function of VGAM1058 is therefore inhibition of

DKFZP566D1346 (Accession NM_030816). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566D1346. DKFZp586H0623 (Accession NM_017540) is another VGAM1058 host target gene. DKFZp586H0623 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586H0623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586H0623 BINDING SITE, designated SEQ ID:18982, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38752] Another function of VGAM1058 is therefore inhibition of DKFZp586H0623 (Accession NM_017540). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586H0623. FLJ11383 (Accession NM_024938) is another VGAM1058 host target gene. FLJ11383 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11383, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11383 BINDING SITE, designated SEQ ID:24478, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38753] Another function of VGAM1058 is therefore inhibition of FLJ11383 (Accession NM_024938). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11383. FLJ20694 (Accession NM_017928) is another VGAM1058 host target gene. FLJ20694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20694 BINDING SITE, designated SEQ ID:19609, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38754] Another function of VGAM1058 is therefore inhibition of FLJ20694 (Accession NM_017928). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ20694. KIAA1691 (Accession XM_166523) is another VGAM1058 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44469, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38755] Another function of VGAM1058 is therefore inhibition of KIAA1691 (Accession XM_166523). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. MGC35558 (Accession NM_145013) is another VGAM1058 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29617, to the nucleotide sequence of VGAM1058 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3769.

[38756] Another function of VGAM1058 is therefore inhibition of MGC35558 (Accession NM_145013). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. PRO1843 (Accession NM_018507) is another VGAM1058 host target gene. PRO1843 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO1843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1843 BINDING SITE, designated SEQ ID:20573, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38757] Another function of VGAM1058 is therefore inhibition of PRO1843 (Accession NM_018507). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1843. SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373) is another VGAM1058 host target gene. SH3BGRL BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by SH3BGRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL BINDING SITE, designated SEQ ID:31025, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38758] Another function of VGAM1058 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL. Zinc Finger Protein 387 (ZNF387, Accession NM_014682) is another VGAM1058 host target gene. ZNF387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF387 BINDING SITE, designated SEQ ID:16177, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38759] Another function of VGAM1058 is therefore inhibition of Zinc Finger Protein 387 (ZNF387, Accession NM_014682). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF387. LOC152627 (Accession XM_087495) is another VGAM1058 host target gene. LOC152627 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39294, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38760] Another function of VGAM1058 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC162333, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42131, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38761] Another function of VGAM1058 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC168082 (Accession XM_094852) is another VGAM1058 host target gene. LOC168082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168082 BINDING SITE, designated SEQ ID:40238, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38762] Another function of VGAM1058 is therefore inhibition of LOC168082 (Accession XM_094852). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC168082. LOC90906 (Accession XM_034809) is another VGAM1058 host target gene. LOC90906 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90906 BINDING SITE, designated SEQ ID:32153, to the nucleotide sequence of VGAM1058 RNA, herein designated VGAM RNA, also designated SEQ ID:3769.

[38763] Another function of VGAM1058 is therefore inhibition of LOC90906 (Accession XM_034809). Accordingly, utilities of VGAM1058 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90906. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1059 (VGAM1059) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38764] VGAM1059 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1059 was detected is described hereinabove with reference to Figs. 1–8.

[38765] VGAM1059 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murid Herpesvirus 4. VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38766] VGAM1059 gene encodes a VGAM1059 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1059 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1059 precursor RNA is designated SEQ ID:1045, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1045 is located at position 97788 relative to the genome of Murid Herpesvirus 4.

[38767] VGAM1059 precursor RNA folds onto itself, forming VGAM1059 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38768] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1059 folded precursor RNA into VGAM1059 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1059 RNA is designated SEQ ID:3770, and is provided hereinbelow with reference to the sequence listing part.

[38769] VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1059 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38770] VGAM1059 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1059 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1059 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38771] The complementary binding of VGAM1059 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1059 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1059 host target RNA into VGAM1059 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38772] It is appreciated that VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1059 host target genes. The mRNA of each one of this plurality of VGAM1059 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1059 RNA, herein designated VGAM RNA, and which when bound by VGAM1059 RNA causes inhibition of translation of respective one or more VGAM1059 host target proteins.

[38773] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1059 gene, herein designated VGAM GENE, on one or more VGAM1059 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38774] It is yet further appreciated that a function of VGAM1059 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1059 correlate with, and may be deduced from, the identity of the host target genes which VGAM1059 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38775] Nucleotide sequences of the VGAM1059 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1059 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1059 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1059 are further described hereinbelow with reference to Table 1.

[38776] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1059 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1059 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38777] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1059 gene, herein designated VGAM is inhibition of expression of VGAM1059 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1059 correlate with, and may be deduced from, the identity of the target genes which VGAM1059 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38778] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 4 (ADAMTS4, Accession NM_005099) is a VGAM1059 host target gene.

ADAMTS4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADAMTS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS4 BINDING SITE, designated SEQ ID:11568, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38779] A function of VGAM1059 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 4 (ADAMTS4, Accession NM_005099), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS4. The function of ADAMTS4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM809. Angiopoietin 1 (ANGPT1, Accession NM_001146) is another VGAM1059 host target gene. ANGPT1 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by ANGPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANGPT1 BINDING SITE, designated SEQ ID:6816, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38780] Another function of VGAM1059 is therefore inhibition of Angiopoietin 1 (ANGPT1, Accession NM_001146), a gene which binds and activates tie2 receptor by inducing its tyrosine phosphorylation. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANGPT1. The function of ANGPT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM291. Cystic Fibrosis Transmembrane Conductance Regulator, ATP-binding Cassette (sub-family C, member 7) (CFTR, Accession NM_000492) is another VGAM1059 host target gene. CFTR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CFTR, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CFTR BINDING SITE, designated SEQ ID:6101, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38781] Another function of VGAM1059 is therefore inhibition of Cystic Fibrosis Transmembrane Conductance Regulator, ATP-binding Cassette (sub-family C, member 7) (CFTR, Accession NM_000492). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CFTR. Glutamate Decarboxylase 1 (brain, 67kDa) (GAD1, Accession NM_000817) is another VGAM1059 host target gene. GAD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAD1 BINDING SITE, designated SEQ ID:6481, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38782] Another function of VGAM1059 is therefore inhibition of

Glutamate Decarboxylase 1 (brain, 67kDa) (GAD1, Accession NM_000817), a gene which catalyzes the conversion of glutamic acid to gamma-aminobutyric acid. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAD1. The function of GAD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM691. Potassium Channel, Subfamily K, Member 3 (KCNK3, Accession NM_002246) is another VGAM1059 host target gene. KCNK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK3 BINDING SITE, designated SEQ ID:8034, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38783] Another function of VGAM1059 is therefore inhibition of Potassium Channel, Subfamily K, Member 3 (KCNK3, Accession NM_002246), a gene which is a pH-dependent, voltage-insensitive, background potassium channel. Ac-

cordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK3. The function of KCNK3 has been established by previous studies. Potassium channels are ubiquitous multisubunit membrane proteins that regulate membrane potential in numerous cell types. One family of mammalian K⁺ channels is characterized by the presence of 4 transmembrane domains and 2 P domains per subunit; this family includes TASK, TWIK (KCNK1; 601745), and TREK (KCNK2; 603219). Duprat et al. (1997) identified mouse expressed sequence tags with similarity to TREK and TWIK and cloned a corresponding cDNA from a mouse brain library. The mouse cDNA was used to clone the human counterpart from a kidney cDNA library. The human cDNA, designated TASK, encodes a 394-amino acid polypeptide with 85% identity to the mouse ortholog. The sequence contains consensus sites for N-linked glycosylation and for phosphorylation at the C-terminal. Northern blot analysis showed that TASK is expressed in a variety of human tissues, with highest levels in pancreas and placenta. Expression of the TASK cDNA revealed that the functional protein creates currents that are K(+)–selective, instantaneous, and noninactivating. These currents

showed an outward rectification when external K⁺ was low, but evinced absence of activation and inactivation kinetics as well as voltage independence, characteristics of so-called leak or background conductances. TASK currents were very sensitive to small changes in extracellular pH, suggesting that TASK has a role in cellular responses to changes in extracellular pH. Lesage and Lazdunski (1998) used a radiation hybrid mapping panel to map the human KCNK3 gene to chromosome 2p23 between markers WI13615 and WI11298. By fluorescence in situ hybridization, Manjunath et al. (1999) mapped the KCNK3 gene to 2p24.1–p23.3 and the mouse homolog to chromosome 5B.

[38784] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38785] Lesage, F.; Lazdunski, M. : Mapping of human potassium channel genes TREK-1 (KCNK2) and TASK (KCNK3) to chromosomes 1q41 and 2p23. *Genomics* 51: 478–479, 1998. ; and

[38786] Manjunath, N. A.; Bray-Ward, P.; Goldstein, S. A. N.; Gallagher, P. G. : Assignment of the 2P domain, acid-sensitive potassium channel OAT1 gene KCNK3 to human

chromosome bands 2p24.1–p.

[38787] Further studies establishing the function and utilities of KCNK3 are found in John Hopkins OMIM database record ID 603220, and in cited publications numbered 243 and 2437 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Antigen P97 (melanoma associated) Identified By Monoclonal Antibodies 133.2 and 96.5 (MFI2, Accession NM_033316) is another VGAM1059 host target gene. MFI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MFI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MFI2 BINDING SITE, designated SEQ ID:27153, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38788] Another function of VGAM1059 is therefore inhibition of Antigen P97 (melanoma associated) Identified By Monoclonal Antibodies 133.2 and 96.5 (MFI2, Accession NM_033316). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFI2. Nuclear Receptor

Coactivator 3 (NCOA3, Accession NM_006534) is another VGAM1059 host target gene. NCOA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCOA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA3 BINDING SITE, designated SEQ ID:13287, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38789] Another function of VGAM1059 is therefore inhibition of Nuclear Receptor Coactivator 3 (NCOA3, Accession NM_006534), a gene which directly binds nuclear receptors and stimulates the transcriptional activities in hormone-dependent fashion. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA3. The function of NCOA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM215. Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269) is another VGAM1059 host target gene. NR2E1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by NR2E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR2E1 BINDING SITE, designated SEQ ID:9279, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38790] Another function of VGAM1059 is therefore inhibition of Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269), a gene which may be required for brain development and be involved in the regulation of retinal development . Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR2E1. The function of NR2E1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM689.Radixin (RDX, Accession NM_002906) is another VGAM1059 host target gene. RDX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDX BINDING SITE, designated SEQ ID:8810, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38791] Another function of VGAM1059 is therefore inhibition of Radixin (RDX, Accession NM_002906), a gene which plays a crucial role in the binding of the barbed end of actin filaments to the plasma membrane. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDX. The function of RDX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM290. Surfeit 4 (SURF4, Accession NM_033161) is another VGAM1059 host target gene. SURF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SURF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SURF4 BINDING SITE, designated SEQ ID:27014, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA,

also designated SEQ ID:3770.

[38792] Another function of VGAM1059 is therefore inhibition of Surfeit 4 (SURF4, Accession NM_033161), a gene which is a conserved integral membrane protein containing multiple putative transmembrane regions. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SURF4. The function of SURF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM496. Ubiquitin-conjugating Enzyme E2L 6 (UBE2L6, Accession NM_004223) is another VGAM1059 host target gene. UBE2L6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2L6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2L6 BINDING SITE, designated SEQ ID:10420, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38793] Another function of VGAM1059 is therefore inhibition of Ubiquitin-conjugating Enzyme E2L 6 (UBE2L6, Accession

NM_004223), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2L6. The function of UBE2L6 has been established by previous studies. Ubiquitination of a protein substrate requires the concerted action of 3 classes of enzymes: E1 ubiquitin-activating enzymes, E2 ubiquitin-conjugating enzymes, and E3 ubiquitin protein ligases. See 600012. E2 enzymes may transfer ubiquitin either directly to a substrate or to an E3 protein. Class I E2s are unable to transfer ubiquitin to proteins in vitro, suggesting that this class of E2s may require an E3 enzyme for substrate recognition. Using a yeast 2-hybrid assay with the E3 enzyme E6AP (OMIM Ref. No. 601623) as bait, Kumar et al. (1997) identified cDNAs encoding a novel class I E2 that they named UBCH8. The predicted 152-amino acid UBCH8 protein is 46% identical to UBCH7 (OMIM Ref. No. 603721). In vitro, recombinant Ubch8 formed thiol ester complexes with ubiquitin and was able to transfer ubiquitin to E6AP. Both UBCH7 and UBCH8 specifically associated with E6AP in yeast 2-hybrid assays, while UBCH5 (OMIM Ref. No. 602961) and UBCH6 (OMIM Ref. No.

602916) interacted selectively with an *S. cerevisiae* E3, RSP5 (see OMIM Ref. No. 602278). In vitro, the E6AP-interacting E2s were also able to function with E6AP in the ubiquitination of a substrate, whereas noninteracting E2s were unable to do so. The authors suggested that selective physical interaction between E2 and E3 enzymes forms the basis of specificity for functionally distinct E2-E3 combinations. By fluorescence in situ hybridization, Ardley et al. (2000) mapped the UBE2L6 gene to chromosome 11q12.

[38794] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38795] Ardley, H. C.; Rose, S. A.; Tan, N.; Leek, J. P.; Markham, A. F.; Robinson, P. A. : Genomic organization of the human ubiquitin-conjugating enzyme gene, UBE2L6 on chromosome 11q12. *Cytogenet. Cell Genet.* 89: 137-140, 2000. ; and

[38796] Kumar, S.; Kao, W. H.; Howley, P. M. : Physical interaction between specific E2 and Hect E3 enzymes determines functional cooperativity. *J. Biol. Chem.* 272: 13548-13554, 1997.

[38797] Further studies establishing the function and utilities of

UBE2L6 are found in John Hopkins OMIM database record ID 603890, and in cited publications numbered 7630–7631 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Vacuolar Protein Sorting 41 (yeast) (VPS41, Accession NM_014396) is another VGAM1059 host target gene. VPS41 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VPS41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS41 BINDING SITE, designated SEQ ID:15738, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38798] Another function of VGAM1059 is therefore inhibition of Vacuolar Protein Sorting 41 (yeast) (VPS41, Accession NM_014396). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS41. BC022889 (Accession XM_096964) is another VGAM1059 host target gene. BC022889 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BC022889, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BC022889 BINDING SITE, designated SEQ ID:40683, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38799] Another function of VGAM1059 is therefore inhibition of BC022889 (Accession XM_096964). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BC022889. DKFZP434P0111 (Accession XM_041116) is another VGAM1059 host target gene. DKFZP434P0111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0111 BINDING SITE, designated SEQ ID:33455, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38800] Another function of VGAM1059 is therefore inhibition of DKFZP434P0111 (Accession XM_041116). Accordingly,

utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0111. F-box Only Protein 9 (FBXO9, Accession NM_033480) is another VGAM1059 host target gene. FBXO9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FBXO9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO9 BINDING SITE, designated SEQ ID:27256, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38801] Another function of VGAM1059 is therefore inhibition of F-box Only Protein 9 (FBXO9, Accession NM_033480). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO9. FLJ00001 (Accession XM_088525) is another VGAM1059 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39787, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38802] Another function of VGAM1059 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ10420 (Accession NM_018090) is another VGAM1059 host target gene. FLJ10420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10420 BINDING SITE, designated SEQ ID:19857, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38803] Another function of VGAM1059 is therefore inhibition of FLJ10420 (Accession NM_018090). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10420. FLJ11175 (Accession NM_018349) is another

VGAM1059 host target gene. FLJ11175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11175 BINDING SITE, designated SEQ ID:20362, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38804] Another function of VGAM1059 is therefore inhibition of FLJ11175 (Accession NM_018349). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11175. FLJ12747 (Accession NM_032173) is another VGAM1059 host target gene. FLJ12747 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12747 BINDING SITE, designated SEQ ID:25879, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38805] Another function of VGAM1059 is therefore inhibition of FLJ12747 (Accession NM_032173). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12747. FLJ22679 (Accession NM_032227) is another VGAM1059 host target gene. FLJ22679 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22679 BINDING SITE, designated SEQ ID:25952, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38806] Another function of VGAM1059 is therefore inhibition of FLJ22679 (Accession NM_032227). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22679. GEMIN7 (Accession NM_024707) is another VGAM1059 host target gene. GEMIN7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GEMIN7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GEMIN7 BINDING SITE, designated SEQ ID:24023, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38807] Another function of VGAM1059 is therefore inhibition of GEMIN7 (Accession NM_024707). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GEMIN7. Hypermethylated In Cancer 2 (HIC2, Accession XM_036937) is another VGAM1059 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32528, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38808] Another function of VGAM1059 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM_036937). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with HIC2. KIAA0237 (Accession NM_014747) is another VGAM1059 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16455, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38809] Another function of VGAM1059 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0459 (Accession XM_027862) is another VGAM1059 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30579, to the

nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38810] Another function of VGAM1059 is therefore inhibition of KIAA0459 (Accession XM_027862). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0459. KIAA0493 (Accession XM_034717) is another VGAM1059 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0493 BINDING SITE, designated SEQ ID:32144, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38811] Another function of VGAM1059 is therefore inhibition of KIAA0493 (Accession XM_034717). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0682 (Accession NM_014852) is another VGAM1059 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:16903, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38812] Another function of VGAM1059 is therefore inhibition of KIAA0682 (Accession NM_014852). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA0763 (Accession NM_014869) is another VGAM1059 host target gene. KIAA0763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0763 BINDING SITE, designated SEQ ID:16968, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38813] Another function of VGAM1059 is therefore inhibition of KIAA0763 (Accession NM_014869). Accordingly, utilities

of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0763. KIAA1463 (Accession XM_051160) is another VGAM1059 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35773, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38814] Another function of VGAM1059 is therefore inhibition of KIAA1463 (Accession XM_051160). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211) is another VGAM1059 host target gene. LOXL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOXL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of LOXL4 BINDING SITE, designated SEQ ID:25926, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38815] Another function of VGAM1059 is therefore inhibition of Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOXL4. MBLL39 (Accession NM_144778) is another VGAM1059 host target gene. MBLL39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBLL39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBLL39 BINDING SITE, designated SEQ ID:29575, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38816] Another function of VGAM1059 is therefore inhibition of MBLL39 (Accession NM_144778). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBLL39. PP2447 (Accession NM_025204) is another

VGAM1059 host target gene. PP2447 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PP2447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP2447 BINDING SITE, designated SEQ ID:24870, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38817] Another function of VGAM1059 is therefore inhibition of PP2447 (Accession NM_025204). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP2447. PRO1331 (Accession NM_030778) is another VGAM1059 host target gene. PRO1331 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1331, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1331 BINDING SITE, designated SEQ ID:25068, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38818] Another function of VGAM1059 is therefore inhibition of PRO1331 (Accession NM_030778). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1331. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942) is another VGAM1059 host target gene. RPS6KA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA4 BINDING SITE, designated SEQ ID:10055, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38819] Another function of VGAM1059 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA4. SCYD1 (Accession XM_165650) is another VGAM1059 host target gene. SCYD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by SCYD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYD1 BINDING SITE, designated SEQ ID:43707, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38820] Another function of VGAM1059 is therefore inhibition of SCYD1 (Accession XM_165650). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYD1. SPARC-like 1 (mast9, hevin) (SPARCL1, Accession NM_004684) is another VGAM1059 host target gene. SPARCL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SPARCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPARCL1 BINDING SITE, designated SEQ ID:11046, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38821] Another function of VGAM1059 is therefore inhibition of

SPARC-like 1 (mast9, hevin) (SPARCL1, Accession NM_004684). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPARCL1. Triple Homeobox 1 (TIX1, Accession XM_029734) is another VGAM1059 host target gene. TIX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIX1 BINDING SITE, designated SEQ ID:30931, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38822] Another function of VGAM1059 is therefore inhibition of Triple Homeobox 1 (TIX1, Accession XM_029734). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIX1. TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256) is another VGAM1059 host target gene. TRAF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF3, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF3 BINDING SITE, designated SEQ ID:30044, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38823] Another function of VGAM1059 is therefore inhibition of TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF3. LOC115219 (Accession XM_055499) is another VGAM1059 host target gene. LOC115219 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115219 BINDING SITE, designated SEQ ID:36278, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38824] Another function of VGAM1059 is therefore inhibition of LOC115219 (Accession XM_055499). Accordingly, utilities

of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115219. LOC133418 (Accession XM_059649) is another VGAM1059 host target gene. LOC133418 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133418 BINDING SITE, designated SEQ ID:37039, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38825] Another function of VGAM1059 is therefore inhibition of LOC133418 (Accession XM_059649). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133418. LOC143173 (Accession XM_016685) is another VGAM1059 host target gene. LOC143173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC143173 BINDING SITE, designated SEQ ID:30273, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38826] Another function of VGAM1059 is therefore inhibition of LOC143173 (Accession XM_016685). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143173. LOC149837 (Accession XM_097747) is another VGAM1059 host target gene. LOC149837 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149837 BINDING SITE, designated SEQ ID:41102, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38827] Another function of VGAM1059 is therefore inhibition of LOC149837 (Accession XM_097747). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149837. LOC150271 (Accession XM_097859) is another VGAM1059 host target gene. LOC150271 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41169, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38828] Another function of VGAM1059 is therefore inhibition of LOC150271 (Accession XM_097859). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC151318 (Accession XM_087170) is another VGAM1059 host target gene. LOC151318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151318 BINDING SITE, designated SEQ ID:39105, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38829] Another function of VGAM1059 is therefore inhibition of

LOC151318 (Accession XM_087170). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151318. LOC158987 (Accession XM_099015) is another VGAM1059 host target gene. LOC158987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158987 BINDING SITE, designated SEQ ID:42050, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38830] Another function of VGAM1059 is therefore inhibition of LOC158987 (Accession XM_099015). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158987. LOC220954 (Accession XM_167628) is another VGAM1059 host target gene. LOC220954 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC220954 BINDING SITE, designated SEQ ID:44737, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38831] Another function of VGAM1059 is therefore inhibition of LOC220954 (Accession XM_167628). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220954. LOC254532 (Accession XM_172961) is another VGAM1059 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46209, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38832] Another function of VGAM1059 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC255598 (Accession XM_173715) is an-

other VGAM1059 host target gene. LOC255598 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255598 BINDING SITE, designated SEQ ID:46559, to the nucleotide sequence of VGAM1059 RNA, herein designated VGAM RNA, also designated SEQ ID:3770.

[38833] Another function of VGAM1059 is therefore inhibition of LOC255598 (Accession XM_173715). Accordingly, utilities of VGAM1059 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255598. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1060 (VGAM1060) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38834] VGAM1060 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1060 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[38835] VGAM1060 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Mop–top Virus.

VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38836] VGAM1060 gene encodes a VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1060 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1060 precursor RNA is designated SEQ ID:1046, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1046 is located at position 2755 relative to the genome of Potato Mop–top Virus.

[38837] VGAM1060 precursor RNA folds onto itself, forming VGAM1060 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38838] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1060 folded precursor RNA into VGAM1060 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1060 RNA is designated SEQ ID:3771, and is provided hereinbelow with reference to the sequence listing part.

[38839] VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1060 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38840] VGAM1060 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1060 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1060 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1060 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38841] The complementary binding of VGAM1060 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1060 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1060 host target RNA into VGAM1060 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38842] It is appreciated that VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1060 host target genes. The mRNA of each one of this plurality of VGAM1060 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1060 RNA, herein designated VGAM RNA, and which when bound by VGAM1060 RNA causes inhibition of translation of respective one or more VGAM1060 host target proteins.

[38843] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1060 gene, herein designated VGAM GENE, on one or more VGAM1060 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38844] It is yet further appreciated that a function of VGAM1060 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of viral infection by Potato Mop-top Virus. Specific functions, and accordingly utilities, of VGAM1060 correlate with, and may be deduced from, the identity of the host target genes which VGAM1060 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38845] Nucleotide sequences of the VGAM1060 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1060 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1060 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1060 are further described hereinbelow with reference to Table 1.

[38846] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1060 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1060 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38847] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1060 gene, herein designated VGAM is inhibition of expression of VGAM1060 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1060 correlate with, and may be deduced from, the identity of the target genes which VGAM1060 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38848] Protocadherin Alpha 1 (PCDHA1, Accession NM_031411) is a VGAM1060 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:25381 and SEQ ID:20862 respectively, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38849] A function of VGAM1060 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_031411). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_031860) is another VGAM1060 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:25613 and SEQ ID:20882 respectively, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38850] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_031860). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM1060 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20903, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38851] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM_018905) is another VGAM1060 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20913, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38852] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM_018905). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM1060 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20923, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38853] Another function of VGAM1060 is therefore inhibition of

Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM1060 host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20933, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38854] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM_018908) is another VGAM1060 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20943, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38855] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM_018908). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM_018909) is another VGAM1060 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:20953 and SEQ ID:25585 respectively, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38856] Another function of VGAM1060 is therefore inhibition of

Protocadherin Alpha 6 (PCDHA6, Accession NM_018909). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM_018911) is another VGAM1060 host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20973, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38857] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 8 (PCDHA8, Accession NM_018911). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM1060 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25598, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38858] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM1060 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated

SEQ ID:20842, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38859] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899) is another VGAM1060 host target gene. PCDHAC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC2 BINDING SITE, designated SEQ ID:20852, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38860] Another function of VGAM1060 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. Replication Pro-

tein A2, 32kDa (RPA2, Accession NM_002946) is another VGAM1060 host target gene. RPA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPA2 BINDING SITE, designated SEQ ID:8857, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38861] Another function of VGAM1060 is therefore inhibition of Replication Protein A2, 32kDa (RPA2, Accession NM_002946). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPA2. FLJ20079 (Accession NM_017656) is another VGAM1060 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19168, to the nucleotide sequence of VGAM1060 RNA,

herein designated VGAM RNA, also designated SEQ ID:3771.

[38862] Another function of VGAM1060 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. G-protein Coupled Receptor 88 (GPR88, Accession NM_022049) is another VGAM1060 host target gene. GPR88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR88 BINDING SITE, designated SEQ ID:22574, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38863] Another function of VGAM1060 is therefore inhibition of G-protein Coupled Receptor 88 (GPR88, Accession NM_022049). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR88. LOC116064 (Accession XM_057296) is another VGAM1060 host target

gene. LOC116064 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116064 BINDING SITE, designated SEQ ID:36498, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38864] Another function of VGAM1060 is therefore inhibition of LOC116064 (Accession XM_057296). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116064. LOC168448 (Accession XM_095105) is another VGAM1060 host target gene. LOC168448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC168448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168448 BINDING SITE, designated SEQ ID:40246, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38865] Another function of VGAM1060 is therefore inhibition of LOC168448 (Accession XM_095105). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168448. LOC220477 (Accession XM_071675) is another VGAM1060 host target gene. LOC220477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220477 BINDING SITE, designated SEQ ID:37411, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38866] Another function of VGAM1060 is therefore inhibition of LOC220477 (Accession XM_071675). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220477. LOC83693 (Accession NM_031463) is another VGAM1060 host target gene. LOC83693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC83693, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC83693 BINDING SITE, designated SEQ ID:25499, to the nucleotide sequence of VGAM1060 RNA, herein designated VGAM RNA, also designated SEQ ID:3771.

[38867] Another function of VGAM1060 is therefore inhibition of LOC83693 (Accession NM_031463). Accordingly, utilities of VGAM1060 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC83693. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1061 (VGAM1061) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38868] VGAM1061 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1061 was detected is described hereinabove with reference to Figs. 1–8.

[38869] VGAM1061 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Adenovirus Type 1. VGAM1061 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[38870] VGAM1061 gene encodes a VGAM1061 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1061 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1061 precursor RNA is designated SEQ ID:1047, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1047 is located at position 7412 relative to the genome of Canine Adenovirus Type 1.

[38871] VGAM1061 precursor RNA folds onto itself, forming VGAM1061 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38872] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1061 folded precursor RNA into VGAM1061

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1061 RNA is designated SEQ ID:3772, and is provided hereinbelow with reference to the sequence listing part.

[38873] VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1061 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38874] VGAM1061 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1061 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1061 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38875] The complementary binding of VGAM1061 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1061 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1061 host target RNA into VGAM1061 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[38876] It is appreciated that VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1061 host target genes. The mRNA of each one of this plurality of VGAM1061 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1061 RNA, herein designated VGAM RNA, and which when bound by VGAM1061 RNA causes inhibition of translation of respective one or more VGAM1061 host target proteins.

[38877] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1061 gene, herein designated VGAM GENE, on one or more VGAM1061 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38878] It is yet further appreciated that a function of VGAM1061 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of viral infection by Canine Adenovirus Type 1. Specific functions, and accordingly utilities, of VGAM1061 correlate with, and may be deduced from, the identity of the host target genes which VGAM1061 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38879] Nucleotide sequences of the VGAM1061 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1061 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1061 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1061 are further described hereinbelow with reference to Table 1.

[38880] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1061 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1061 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38881] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1061 gene, herein designated VGAM is inhibition of expression of VGAM1061 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1061 correlate with, and may be deduced from, the identity of the target genes which VGAM1061 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38882] Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM_171045) is a VGAM1061 host target gene. IHPK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK1 BINDING SITE, designated SEQ ID:45821, to the nucleotide sequence of VGAM1061 RNA, herein designated

VGAM RNA, also designated SEQ ID:3772.

[38883] A function of VGAM1061 is therefore inhibition of Inositol Hexaphosphate Kinase 1 (IHPK1, Accession XM_171045), a gene which is a messenger molecule that releases calcium from intracellular stores. Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK1. The function of IHPK1 has been established by previous studies. Inositol trisphosphate is a messenger molecule that releases calcium from intracellular stores. Homologs with multiple phosphates, including pyrophosphates, have also been identified. Inositol pyrophosphates are formed by several enzymes, including IHPK1. By screening an immature myeloid cell line for cDNAs with the potential to encode large proteins, Nagase et al. (1996) identified a cDNA encoding IHPK1, which they called KIAA0263, a deduced 462-amino acid protein. Northern blot analysis detected ubiquitous, low-level expression that was highest in testis. By comparison with rat *lhpk1* and database searching, Saiardi et al. (1999) identified mouse *lhpk1*, which is 97% homologous to KIAA0263. Western blot analysis showed expression of a 50-kD protein. Northern blot analysis revealed expression of a 5.0-kb transcript in

mouse brain and testis, with much lower levels in heart, liver, kidney, lung, and spleen. Using confocal microscopy, Saiardi et al. (2001) demonstrated that mouse Ihpk1 is present in both the nucleus and the cytoplasm, whereas IHPK2 is almost exclusively nuclear and IHPK3 (OMIM Ref. No. 606993) is predominantly cytoplasmic. Saiardi et al. (1999) showed that cells expressing Ihpk1 displayed a robust InsP6 kinase activity. They proposed that IHPK1 and IHPK2 (OMIM Ref. No. 606992) may act as energy reserves in selected intracellular sites.

[38884] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38885] Saiardi, A.; Erdjument-Bromage, H.; Snowman, A. M.; Tempst, P.; Snyder, S. H. : Synthesis of diphosphoinositol pentakisphosphate by a newly identified family of higher inositol polyphosphate kinases. *Curr. Biol.* 9: 1323–1326, 1999. ; and

[38886] Saiardi, A.; Nagata, E.; Luo, H. R.; Snowman, A. M.; Snyder, S. H. : Identification and characterization of a novel inositol hexakisphosphate kinase. *J. Biol. Chem.* 276: 39179–39185, 20.

[38887] Further studies establishing the function and utilities of

IHPK1 are found in John Hopkins OMIM database record ID 606991, and in cited publications numbered 9011–6162 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Muscleblind-like (Drosophila) (MBNL, Accession NM_021038) is another VGAM1061 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBNL BINDING SITE, designated SEQ ID:22032, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38888] Another function of VGAM1061 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM95.SET Translocation (myeloid leukemia-associated) (SET, Accession NM_003011) is another VGAM1061 host target gene. SET BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SET, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SET BINDING SITE, designated SEQ ID:8922, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38889] Another function of VGAM1061 is therefore inhibition of SET Translocation (myeloid leukemia-associated) (SET, Accession NM_003011). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SET. Zinc Finger Protein 219 (ZNF219, Accession NM_016423) is another VGAM1061 host target gene. ZNF219 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

ZNF219 BINDING SITE, designated SEQ ID:18546, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38890] Another function of VGAM1061 is therefore inhibition of Zinc Finger Protein 219 (ZNF219, Accession NM_016423). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF219. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375) is another VGAM1061 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33511, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38891] Another function of VGAM1061 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. ETAA16

(Accession NM_019002) is another VGAM1061 host target gene. ETAA16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ETAA16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ETAA16 BINDING SITE, designated SEQ ID:21073, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38892] Another function of VGAM1061 is therefore inhibition of ETAA16 (Accession NM_019002). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETAA16. FLJ21736 (Accession NM_024922) is another VGAM1061 host target gene. FLJ21736 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21736, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21736 BINDING SITE, designated SEQ ID:24459, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM

RNA, also designated SEQ ID:3772.

[38893] Another function of VGAM1061 is therefore inhibition of FLJ21736 (Accession NM_024922). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21736. KIAA0420 (Accession XM_032693) is another VGAM1061 host target gene. KIAA0420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0420 BINDING SITE, designated SEQ ID:31724, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38894] Another function of VGAM1061 is therefore inhibition of KIAA0420 (Accession XM_032693). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0420. KIAA0644 (Accession NM_014817) is another VGAM1061 host target gene. KIAA0644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0644, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0644 BINDING SITE, designated SEQ ID:16782, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38895] Another function of VGAM1061 is therefore inhibition of KIAA0644 (Accession NM_014817). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0644. KIAA1796 (Accession XM_166146) is another VGAM1061 host target gene. KIAA1796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1796 BINDING SITE, designated SEQ ID:43965, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38896] Another function of VGAM1061 is therefore inhibition of KIAA1796 (Accession XM_166146). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1796. Myristoylated Alanine-rich Protein Kinase C Substrate (MARCKS, Accession NM_002356) is another VGAM1061 host target gene. MARCKS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MARCKS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MARCKS BINDING SITE, designated SEQ ID:8168, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38897] Another function of VGAM1061 is therefore inhibition of Myristoylated Alanine-rich Protein Kinase C Substrate (MARCKS, Accession NM_002356). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MARCKS. MGC15634 (Accession NM_032755) is another VGAM1061 host target gene. MGC15634 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC15634 BINDING SITE, designated SEQ ID:26496, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38898] Another function of VGAM1061 is therefore inhibition of MGC15634 (Accession NM_032755). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15634. LOC130497 (Accession XM_059439) is another VGAM1061 host target gene. LOC130497 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130497 BINDING SITE, designated SEQ ID:36992, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38899] Another function of VGAM1061 is therefore inhibition of LOC130497 (Accession XM_059439). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130497. LOC133418 (Accession XM_059649) is an-

other VGAM1061 host target gene. LOC133418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133418 BINDING SITE, designated SEQ ID:37040, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38900] Another function of VGAM1061 is therefore inhibition of LOC133418 (Accession XM_059649). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133418. LOC144231 (Accession XM_096561) is another VGAM1061 host target gene. LOC144231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144231 BINDING SITE, designated SEQ ID:40390, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38901] Another function of VGAM1061 is therefore inhibition of LOC144231 (Accession XM_096561). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144231. LOC152426 (Accession XM_098225) is another VGAM1061 host target gene. LOC152426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152426 BINDING SITE, designated SEQ ID:41497, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38902] Another function of VGAM1061 is therefore inhibition of LOC152426 (Accession XM_098225). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152426. LOC165693 (Accession XM_093373) is another VGAM1061 host target gene. LOC165693 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165693, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165693 BINDING SITE, designated SEQ ID:40190, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38903] Another function of VGAM1061 is therefore inhibition of LOC165693 (Accession XM_093373). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165693. LOC221895 (Accession XM_166511) is another VGAM1061 host target gene. LOC221895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221895 BINDING SITE, designated SEQ ID:44443, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38904] Another function of VGAM1061 is therefore inhibition of LOC221895 (Accession XM_166511). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221895. LOC257354 (Accession XM_170810) is another VGAM1061 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45577, to the nucleotide sequence of VGAM1061 RNA, herein designated VGAM RNA, also designated SEQ ID:3772.

[38905] Another function of VGAM1061 is therefore inhibition of LOC257354 (Accession XM_170810). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. LOC257476 (Accession XM_028610) is another VGAM1061 host target gene. LOC257476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257476 BINDING SITE, designated SEQ ID:30713, to the nucleotide sequence of VGAM1061 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3772.

[38906] Another function of VGAM1061 is therefore inhibition of LOC257476 (Accession XM_028610). Accordingly, utilities of VGAM1061 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257476. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1062 (VGAM1062) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38907] VGAM1062 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1062 was detected is described hereinabove with reference to Figs. 1–8.

[38908] VGAM1062 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Canine Adenovirus Type 1. VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38909] VGAM1062 gene encodes a VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1062 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1062 precursor RNA is designated SEQ ID:1048, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1048 is located at position 6331 relative to the genome of Canine Adenovirus Type 1.

[38910] VGAM1062 precursor RNA folds onto itself, forming VGAM1062 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38911] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1062 folded precursor RNA into VGAM1062 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1062 RNA is designated SEQ ID:3773, and is provided hereinbelow with reference to the sequence listing part.

[38912] VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1062 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38913] VGAM1062 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1062 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1062 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38914] The complementary binding of VGAM1062 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1062 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1062 host target RNA into VGAM1062 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38915] It is appreciated that VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1062 host target genes. The mRNA of

each one of this plurality of VGAM1062 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1062 RNA, herein designated VGAM RNA, and which when bound by VGAM1062 RNA causes inhibition of translation of respective one or more VGAM1062 host target proteins.

[38916] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1062 gene, herein designated VGAM GENE, on one or more VGAM1062 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[38917] It is yet further appreciated that a function of VGAM1062 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1062 include diagnosis, prevention and treatment of viral infection by Canine Adenovirus Type 1. Specific functions, and accordingly utilities, of VGAM1062 correlate with, and may be deduced from, the identity of the host target genes which VGAM1062 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38918] Nucleotide sequences of the VGAM1062 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1062 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1062 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1062 are further described hereinbelow with reference to Table 1.

[38919] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1062 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1062 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38920] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1062 gene, herein designated VGAM is inhibition of expression of VGAM1062 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1062 correlate with, and may be deduced from, the identity of the target genes which VGAM1062 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38921] Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM_002709) is a VGAM1062 host target gene. PPP1CB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1CB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1CB BINDING SITE, designated SEQ ID:8562, to the nucleotide sequence of VGAM1062 RNA, herein designated VGAM RNA, also designated SEQ ID:3773.

[38922] A function of VGAM1062 is therefore inhibition of Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB,

Accession NM_002709), a gene which is the catalytic subunit of protein phosphatase 1. Accordingly, utilities of VGAM1062 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1CB. The function of PPP1CB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM46.PRO0082 (Accession NM_018590) is another VGAM1062 host target gene. PRO0082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0082 BINDING SITE, designated SEQ ID:20669, to the nucleotide sequence of VGAM1062 RNA, herein designated VGAM RNA, also designated SEQ ID:3773.

[38923] Another function of VGAM1062 is therefore inhibition of PRO0082 (Accession NM_018590). Accordingly, utilities of VGAM1062 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0082. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1063 (VGAM1063) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38924] VGAM1063 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1063 was detected is described hereinabove with reference to Figs. 1–8.

[38925] VGAM1063 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tulip Virus X. VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[38926] VGAM1063 gene encodes a VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1063 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1063 precursor RNA is designated SEQ ID:1049, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1049 is located at position 2404 relative to the

genome of Tulip Virus X.

[38927] VGAM1063 precursor RNA folds onto itself, forming VGAM1063 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[38928] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1063 folded precursor RNA into VGAM1063 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1063 RNA is designated SEQ ID:3774, and is provided hereinbelow with reference to the sequence listing part.

[38929] VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1063 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[38930] VGAM1063 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1063 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1063 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[38931] The complementary binding of VGAM1063 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1063 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1063 host target RNA into VGAM1063 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[38932] It is appreciated that VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1063 host target genes. The mRNA of each one of this plurality of VGAM1063 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1063 RNA, herein designated VGAM RNA, and which when bound by VGAM1063 RNA causes inhibition of translation of respective one or more VGAM1063 host target proteins.

[38933] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1063 gene, herein designated VGAM GENE, on one or more VGAM1063 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[38934] It is yet further appreciated that a function of VGAM1063 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of viral infection by Tulip Virus X. Specific functions, and accordingly utilities, of VGAM1063 correlate

with, and may be deduced from, the identity of the host target genes which VGAM1063 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[38935] Nucleotide sequences of the VGAM1063 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1063 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1063 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1063 are further described hereinbelow with reference to Table 1.

[38936] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1063 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1063 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[38937] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1063 gene, herein designated VGAM is inhibition of expression of VGAM1063 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1063 correlate with, and may be deduced

from, the identity of the target genes which VGAM1063 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[38938] Agrin (AGRN, Accession XM_086178) is a VGAM1063 host target gene. AGRN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AGRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGRN BINDING SITE, designated SEQ ID:38534, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38939] A function of VGAM1063 is therefore inhibition of Agrin (AGRN, Accession XM_086178), a gene which a neuronal aggregating factor that induces the aggregation of acetylcholine receptors . Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGRN. The function of AGRN has been established by previous studies. Agrin is a neuronal aggregating factor that induces the aggregation of acetylcholine receptors and other postsynaptic proteins on muscle fibers and is crucial for the formation of the

neuromuscular junction. Rupp et al. (1991) isolated cDNAs from a rat embryonic spinal cord library using an agrin cDNA clone isolated from electromotor neurons of a marine ray. Analysis of a set of clones predicted a protein with 1,940 amino acids, including 141 cysteine residues. The predicted protein had 9 domains homologous to protease inhibitors, a region similar to domain III of laminin (see OMIM Ref. No. 150240), and 4 epidermal growth factor (OMIM Ref. No. 131530) repeats. The gene was expressed in rat embryonic nervous system and muscle. The protein was concentrated at synapses. Rupp et al. (1992) described alternative RNA splicing in mammalian agrin resulting in many extracellular matrix protein isoforms. Rupp et al. (1992) mapped the human AGRN gene to 1pter-p32 by analysis of Chinese hamster/human somatic cell hybrids, including one that carried chromosome 1 region p32-qter (which was negative for the human signal). The mouse gene was mapped to chromosome 4 by study of Chinese hamster/mouse somatic cell hybrids. Thus, this is another example of extensive homology of synteny between 1pter-p32 and the distal half of mouse chromosome 4. Three neurologic mutants in that region of mouse chromosome 4 were pointed to as possible candidate dis-

eases for mutations in the Agrn gene. Animal model experiments lend further support to the function of AGRN. To test critically the 'agrin hypothesis' (McMahan, 1990), Gautam et al. (1996) generated knockout mice deficient for agrin and showed that neuromuscular differentiation is grossly defective in these mice.

[38940] It is appreciated that the abovementioned animal model for AGRN is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[38941] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38942] Rupp, F.; Payan, D. G.; Magill-Solc, C.; Cowan, D. M.; Scheller, R. H. : Structure and expression of a rat agrin. Neuron 6: 811-823, 1991. ; and

[38943] Gautam, M.; Noakes, P. G.; Moscoso, L.; Rupp, F.; Scheller, R. H.; Merlie, J. P.; Sanes, J. R. : Defective neuromuscular synaptogenesis in agrin-deficient mutant mice. Cell 85: 525-535.

[38944] Further studies establishing the function and utilities of AGRN are found in John Hopkins OMIM database record ID 103320, and in cited publications numbered 11875-1187

and 12115–12121 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774) is another VGAM1063 host target gene. ANK1 BINDING SITE1 through ANK1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE1 through ANK1 BINDING SITE3, designated SEQ ID:30280, SEQ ID:21729 and SEQ ID:5476 respectively, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38945] Another function of VGAM1063 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. E74-like Factor 3 (ets domain transcription factor, epithelial-specific) (ELF3, Accession NM_004433) is another VGAM1063 host target gene. ELF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELF3, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF3 BINDING SITE, designated SEQ ID:10719, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38946] Another function of VGAM1063 is therefore inhibition of E74-like Factor 3 (ets domain transcription factor, epithelial-specific) (ELF3, Accession NM_004433), a gene which is a transcription factor known to be exclusively expressed in epithelial cells. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF3. The function of ELF3 has been established by previous studies. Oettgen et al. (1997) isolated and characterized a novel member of the ETS transcription factor family (see OMIM Ref. No. 164720), which they called ESX (also known as ESS-E). This was the first ETS factor and one of only a few transcription factors known to be exclusively expressed in epithelial cells. ESX contains 2 putative DNA-binding domains: an ETS domain and an A/T hook domain. Oettgen et al. (1999) determined that the ELF3 gene contains 9 exons spanning approximately 5.8 kb of ge-

omic DNA. By fluorescence in situ hybridization (FISH), Oettgen et al. (1997) mapped the ESX gene to 1q32. By the same method, Tymms et al. (1997) refined the location to 1q32.2.

[38947] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38948] Oettgen, P.; Alani, R. M.; Barcinski, M. A.; Brown, L.; Akbarali, Y.; Boltax, J.; Kunsch, C.; Munger, K.; Liebermann, T. A. : Isolation and characterization of a novel epithelium-specific transcription factor, ESE-1, a member of the Ets family. *Molec. Cell. Biol.* 17: 4419-4433, 1997. ; and

[38949] Oettgen, P.; Barcinski, M.; Boltax, J.; Stolt, P.; Akbarali, Y.; Liebermann, T. A. : Genomic organization of the human ELF3 (ESE-1/ESX) gene, a member of the Ets transcription factor fami.

[38950] Further studies establishing the function and utilities of ELF3 are found in John Hopkins OMIM database record ID 602191, and in cited publications numbered 5847-584 and 5851 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibronectin 1 (FN1, Accession NM_002026) is another VGAM1063 host target gene. FN1 BINDING SITE1

and FN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FN1 BINDING SITE1 and FN1 BINDING SITE2, designated SEQ ID:7778 and SEQ ID:27644 respectively, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38951] Another function of VGAM1063 is therefore inhibition of Fibronectin 1 (FN1, Accession NM_002026), a gene which binds cell surfaces and various compounds including collagen, fibrin, heparin, dna, and actin. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FN1. The function of FN1 has been established by previous studies. Fibronectin deficiency has been identified in association with a form of the Ehlers–Danlos syndrome (OMIM Ref. No. type X); see 225310. Is the mutation in that disorder at the locus referred to here? Shirakami et al. (1986) reported plasma fibronectin deficiency in 8 members of 1 family. Enzyme levels were about half–normal in the deficient persons, who were distributed in 3 genera–

tions and 4 sibships in a regular autosomal dominant pattern with male-to-male transmission. The proband, a 31-year-old woman, had keloids at sites of surgery and burns but no other abnormalities; no keloids were found in the deficient relatives. Specifically, there was no unusual susceptibility to infections, bleeding diathesis, or hyperextensibility of joints or skin (see OMIM Ref. No. 225310). No homozygote was definitely demonstrated; a possible homozygote with first-cousin parents died soon after birth. Animal model experiments lend further support to the function of FN1. To investigate the role of plasma fibronectin in vivo, Sakai et al. (2001) generated plasma fibronectin-deficient adult mice using Cre-loxP conditional gene-knockout technology. Sakai et al. (2001) demonstrated that plasma fibronectin-deficient mice show increased neuronal apoptosis and larger infarction areas following transient focal cerebral ischemia. Surprisingly, plasma fibronectin is not essential for skin-wound healing or hemostasis.

[38952] It is appreciated that the abovementioned animal model for FN1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[38953] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38954] Sakai, T.; Johnson, K. J.; Murozono, M.; Sakai, K.; Magnusson, M. A.; Wieloch, T.; Cronberg, T.; Isshiki, A.; Erickson, H. P.; Fassler, R. : Plasma fibronectin supports neuronal survival and reduces brain injury following transient focal cerebral ischemia but is not essential for skin-wound healing and hemostasis. *Nature Med.* 7: 324–330, 2001. ; and

[38955] Shirakami, A.; Shigekiyo, T.; Hirai, Y.; Takeichi, T.; Kawauchi, S.; Saito, S.; Miyoshi, K. : Plasma fibronectin deficiency in eight members of one family. *Lancet I*: 473–474, 1986.

[38956] Further studies establishing the function and utilities of FN1 are found in John Hopkins OMIM database record ID 135600, and in cited publications numbered 2153–2176, 878, 3324–333 and 12153 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Heparan Sulfate 2–O–sulfotransferase 1 (HS2ST1, Accession NM_012262) is another VGAM1063 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14574, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38957] Another function of VGAM1063 is therefore inhibition of Heparan Sulfate 2-O-sulfotransferase 1 (HS2ST1, Accession NM_012262). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS2ST1. Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3, Accession NM_005501) is another VGAM1063 host target gene. ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ITGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2, designated SEQ ID:12008 and SEQ ID:7965 respectively, to the nucleotide sequence of VGAM1063 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3774.

[38958] Another function of VGAM1063 is therefore inhibition of Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3, Accession NM_005501), a gene which is a receptor for fibronectin, laminin, collagen, epiligrin and thrombospondin. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA3. The function of ITGA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1020. Polymerase (RNA) II (DNA directed) Polypeptide E, 25kDa (POLR2E, Accession XM_009279) is another VGAM1063 host target gene. POLR2E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLR2E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLR2E BINDING SITE, designated SEQ ID:30107, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38959] Another function of VGAM1063 is therefore inhibition of

Polymerase (RNA) II (DNA directed) Polypeptide E, 25kDa (POLR2E, Accession XM_009279), a gene which is a subunit of a DNA-dependent RNA polymerase. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLR2E. The function of POLR2E has been established by previous studies. Acker et al. (1994) isolated cDNAs of 5 subunits of RNA polymerase II. Cramer et al. (2000) derived a backbone model of a 10-subunit yeast RNA polymerase II using x-ray diffraction data extending to 3-angstrom resolution. All 10 subunits exhibited a high degree of identity with the corresponding human proteins, and 9 of the 10 subunits are conserved among the 3 eukaryotic RNA polymerases I, II, and III. Notable features of the model include a pair of jaws, formed by subunits Rpb1 (OMIM Ref. No. 180660), Rpb5 (homologous to human POLR2E), and Rpb9 (OMIM Ref. No. 180662), that appear to grip DNA downstream of the active center. A clamp on the DNA nearer the active center, formed by Rpb1, Rpb2 (OMIM Ref. No. 180661), and Rpb6 (OMIM Ref. No. 604414), may be locked in the closed position by RNA, accounting for the great stability of transcribing complexes. A pore in the protein complex be-

neath the active center may allow entry of substrates for polymerization and exit of the transcript during proof-reading and passage through pause sites in the DNA.

[38960] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[38961] Acker, J.; Mattei, M.-G.; Wintzerith, M.; Roeckel, N.; Depetris, D.; Vigneron, M.; Kedinger, C. : Chromosomal localization of human RNA polymerase II subunit genes. *Genomics* 20: 496-499, 1994. ; and

[38962] Cramer, P.; Bushnell, D. A.; Fu, J.; Gnatt, A. L.; Maier-Davis, B.; Thompson, N. E.; Burgess, R. R.; Edwards, A. M.; David, P. R.; Kornberg, R. D. : Architecture of RNA polymerase II and im.

[38963] Further studies establishing the function and utilities of POLR2E are found in John Hopkins OMIM database record ID 180664, and in cited publications numbered 12398 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession NM_002933) is another VGAM1063 host target gene. RNASE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

RNASE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNASE1 BINDING SITE, designated SEQ ID:8835, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38964] Another function of VGAM1063 is therefore inhibition of Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession NM_002933), a gene which is a Pancreatic ribonuclease; a pyrimidine-specific endonuclease that generates 2',3'-cyclic phosphate products. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNASE1. The function of RNASE1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210.SH3-domain GRB2-like 1 (SH3GL1, Accession NM_003025) is another VGAM1063 host target gene. SH3GL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3GL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SH3GL1 BINDING SITE, designated SEQ ID:8961, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38965] Another function of VGAM1063 is therefore inhibition of SH3-domain GRB2-like 1 (SH3GL1, Accession NM_003025). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3GL1. SH3 and Multiple Ankyrin Repeat Domains 2 (SHANK2, Accession NM_133266) is another VGAM1063 host target gene. SHANK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHANK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHANK2 BINDING SITE, designated SEQ ID:28421, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38966] Another function of VGAM1063 is therefore inhibition of SH3 and Multiple Ankyrin Repeat Domains 2 (SHANK2, Ac-

cession NM_133266). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHANK2. Solute Carrier Family 4, Anion Exchanger, Member 1 (erythrocyte membrane protein band 3, Diego blood group) (SLC4A1, Accession NM_000342) is another VGAM1063 host target gene. SLC4A1 BINDING SITE1 and SLC4A1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC4A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A1 BINDING SITE1 and SLC4A1 BINDING SITE2, designated SEQ ID:5893 and SEQ ID:5894 respectively, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38967] Another function of VGAM1063 is therefore inhibition of Solute Carrier Family 4, Anion Exchanger, Member 1 (erythrocyte membrane protein band 3, Diego blood group) (SLC4A1, Accession NM_000342). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A1. SORCS2 (Accession NM_020777) is another

VGAM1063 host target gene. SORCS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SORCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS2 BINDING SITE, designated SEQ ID:21875, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38968] Another function of VGAM1063 is therefore inhibition of SORCS2 (Accession NM_020777). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS2. SORCS3 (Accession NM_014978) is another VGAM1063 host target gene. SORCS3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SORCS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS3 BINDING SITE, designated SEQ ID:17363, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38969] Another function of VGAM1063 is therefore inhibition of SORCS3 (Accession NM_014978). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS3. Suppression of Tumorigenicity 7 (ST7, Accession NM_021908) is another VGAM1063 host target gene. ST7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ST7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7 BINDING SITE, designated SEQ ID:22429, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38970] Another function of VGAM1063 is therefore inhibition of Suppression of Tumorigenicity 7 (ST7, Accession NM_021908), a gene which has a role in regulating cell-environment or cell-cell interactions. Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7. The function of ST7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM107.APELIN (Accession NM_017413) is another VGAM1063 host target gene. APELIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APELIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APELIN BINDING SITE, designated SEQ ID:18871, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38971] Another function of VGAM1063 is therefore inhibition of APELIN (Accession NM_017413). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APELIN. Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605) is another VGAM1063 host target gene. C5orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf6 BINDING SITE, designated SEQ ID:18701, to the nucleotide sequence of VGAM1063 RNA,

herein designated VGAM RNA, also designated SEQ ID:3774.

[38972] Another function of VGAM1063 is therefore inhibition of Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf6. DJ37E16.5 (Accession NM_020315) is another VGAM1063 host target gene. DJ37E16.5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ37E16.5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ37E16.5 BINDING SITE, designated SEQ ID:21575, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38973] Another function of VGAM1063 is therefore inhibition of DJ37E16.5 (Accession NM_020315). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ37E16.5. DKFZP434L1435 (Accession XM_166401) is another VGAM1063 host target gene. DKFZP434L1435

BINDING SITE1 through DKFZP434L1435 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434L1435, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L1435 BINDING SITE1 through DKFZP434L1435 BINDING SITE3, designated SEQ ID:44267, SEQ ID:46664 and SEQ ID:46702 respectively, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38974] Another function of VGAM1063 is therefore inhibition of DKFZP434L1435 (Accession XM_166401). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L1435. FLJ10074 (Accession NM_017988) is another VGAM1063 host target gene. FLJ10074 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10074 BINDING SITE, designated SEQ ID:19719, to the

nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38975] Another function of VGAM1063 is therefore inhibition of FLJ10074 (Accession NM_017988). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10074. FLJ13204 (Accession NM_024761) is another VGAM1063 host target gene. FLJ13204 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13204 BINDING SITE, designated SEQ ID:24116, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38976] Another function of VGAM1063 is therefore inhibition of FLJ13204 (Accession NM_024761). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13204. FLJ22671 (Accession NM_024861) is another VGAM1063 host target gene. FLJ22671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22671 BINDING SITE, designated SEQ ID:24294, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38977] Another function of VGAM1063 is therefore inhibition of FLJ22671 (Accession NM_024861). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22671. Glycoprotein V (platelet) (GP5, Accession NM_004488) is another VGAM1063 host target gene. GP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GP5 BINDING SITE, designated SEQ ID:10817, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38978] Another function of VGAM1063 is therefore inhibition of Glycoprotein V (platelet) (GP5, Accession NM_004488).

Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GP5. KIAA0296 (Accession NM_014699) is another VGAM1063 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16220, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38979] Another function of VGAM1063 is therefore inhibition of KIAA0296 (Accession NM_014699). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. KIAA0429 (Accession NM_014751) is another VGAM1063 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16469, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38980] Another function of VGAM1063 is therefore inhibition of KIAA0429 (Accession NM_014751). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. KIAA1193 (Accession XM_041843) is another VGAM1063 host target gene. KIAA1193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE, designated SEQ ID:33580, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38981] Another function of VGAM1063 is therefore inhibition of KIAA1193 (Accession XM_041843). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. KIAA1322 (Accession XM_052626) is another

VGAM1063 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36024, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38982] Another function of VGAM1063 is therefore inhibition of KIAA1322 (Accession XM_052626). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1813 (Accession XM_046743) is another VGAM1063 host target gene. KIAA1813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1813 BINDING SITE, designated SEQ ID:34810, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38983] Another function of VGAM1063 is therefore inhibition of KIAA1813 (Accession XM_046743). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1813. MGC19556 (Accession NM_033551) is another VGAM1063 host target gene. MGC19556 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC19556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC19556 BINDING SITE, designated SEQ ID:27316, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38984] Another function of VGAM1063 is therefore inhibition of MGC19556 (Accession NM_033551). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC19556. MGC2780 (Accession NM_025266) is another VGAM1063 host target gene. MGC2780 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2780, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2780 BINDING SITE, designated SEQ ID:24934, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38985] Another function of VGAM1063 is therefore inhibition of MGC2780 (Accession NM_025266). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2780. Phosphatase, Orphan 1 (phospho1, Accession XM_091572) is another VGAM1063 host target gene. phospho1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by phospho1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of phospho1 BINDING SITE, designated SEQ ID:40061, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38986] Another function of VGAM1063 is therefore inhibition of Phosphatase, Orphan 1 (phospho1, Accession XM_091572). Accordingly, utilities of VGAM1063 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with phospho1. SNRK (Accession NM_017719) is another VGAM1063 host target gene.

SNRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNRK BINDING SITE, designated SEQ ID:19309, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38987] Another function of VGAM1063 is therefore inhibition of SNRK (Accession NM_017719). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNRK. Torsin Family 2, Member A (TOR2A, Accession NM_130459) is another VGAM1063 host target gene. TOR2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOR2A BINDING SITE, designated SEQ

ID:28218, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38988] Another function of VGAM1063 is therefore inhibition of Torsin Family 2, Member A (TOR2A, Accession NM_130459). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOR2A. Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285) is another VGAM1063 host target gene. TP53INP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TP53INP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53INP1 BINDING SITE, designated SEQ ID:27106, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38989] Another function of VGAM1063 is therefore inhibition of Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with TP53INP1. Zinc Finger Protein 304 (ZNF304, Accession NM_020657) is another VGAM1063 host target gene. ZNF304 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF304, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF304 BINDING SITE, designated SEQ ID:21829, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38990] Another function of VGAM1063 is therefore inhibition of Zinc Finger Protein 304 (ZNF304, Accession NM_020657). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF304. LOC146733 (Accession XM_097076) is another VGAM1063 host target gene. LOC146733 BINDING SITE1 and LOC146733 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146733, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC146733 BINDING SITE1 and LOC146733 BINDING SITE2, designated SEQ ID:40727 and SEQ ID:40728 respectively, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38991] Another function of VGAM1063 is therefore inhibition of LOC146733 (Accession XM_097076). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146733. LOC157931 (Accession XM_098845) is another VGAM1063 host target gene. LOC157931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157931 BINDING SITE, designated SEQ ID:41902, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38992] Another function of VGAM1063 is therefore inhibition of LOC157931 (Accession XM_098845). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC157931. LOC166341 (Accession XM_093804) is another VGAM1063 host target gene. LOC166341 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC166341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166341 BINDING SITE, designated SEQ ID:40212, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38993] Another function of VGAM1063 is therefore inhibition of LOC166341 (Accession XM_093804). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166341. LOC220020 (Accession XM_167821) is another VGAM1063 host target gene. LOC220020 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220020 BINDING SITE, designated SEQ ID:44863, to

the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38994] Another function of VGAM1063 is therefore inhibition of LOC220020 (Accession XM_167821). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220020. LOC222070 (Accession XM_168433) is another VGAM1063 host target gene. LOC222070 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222070 BINDING SITE, designated SEQ ID:45178, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38995] Another function of VGAM1063 is therefore inhibition of LOC222070 (Accession XM_168433). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222070. LOC257490 (Accession XM_175163) is another VGAM1063 host target gene. LOC257490 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC257490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257490 BINDING SITE, designated SEQ ID:46647, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38996] Another function of VGAM1063 is therefore inhibition of LOC257490 (Accession XM_175163). Accordingly, utilities of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257490. LOC90784 (Accession XM_034109) is another VGAM1063 host target gene. LOC90784 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90784 BINDING SITE, designated SEQ ID:32004, to the nucleotide sequence of VGAM1063 RNA, herein designated VGAM RNA, also designated SEQ ID:3774.

[38997] Another function of VGAM1063 is therefore inhibition of LOC90784 (Accession XM_034109). Accordingly, utilities

of VGAM1063 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90784. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1064 (VGAM1064) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[38998] VGAM1064 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1064 was detected is described hereinabove with reference to Figs. 1-8.

[38999] VGAM1064 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tulip Virus X. VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39000] VGAM1064 gene encodes a VGAM1064 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1064 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1064 precursor RNA is designated SEQ ID:1050, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1050 is located at position 3436 relative to the genome of Tulip Virus X.

- [39001] VGAM1064 precursor RNA folds onto itself, forming VGAM1064 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39002] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1064 folded precursor RNA into VGAM1064 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1064 RNA is designated SEQ ID:3775, and

is provided hereinbelow with reference to the sequence listing part.

[39003] VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1064 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[39004] VGAM1064 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1064 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1064 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39005] The complementary binding of VGAM1064 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1064 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1064 host target RNA into VGAM1064 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39006] It is appreciated that VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1064 host target genes. The mRNA of each one of this plurality of VGAM1064 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1064 RNA, herein designated VGAM RNA, and which when bound by VGAM1064 RNA causes inhibition of translation of respective one or more VGAM1064 host target proteins.

[39007] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1064 gene, herein designated VGAM GENE, on one or more VGAM1064 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39008] It is yet further appreciated that a function of VGAM1064 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of viral infection by Tulip Virus X. Specific functions, and accordingly utilities, of VGAM1064 correlate with, and may be deduced from, the identity of the host target genes which VGAM1064 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39009] Nucleotide sequences of the VGAM1064 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1064 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1064 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1064 are further described hereinbelow with reference to Table 1.

[39010] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1064 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1064 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39011] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1064 gene, herein designated VGAM is inhibition of expression of VGAM1064 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1064 correlate with, and may be deduced from, the identity of the target genes which VGAM1064 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39012] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM_004776) is a VGAM1064 host target gene. B4GALT5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT5 BINDING SITE, designated SEQ ID:11165, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39013] A function of VGAM1064 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 5 (B4GALT5, Accession NM_004776). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with B4GALT5. NIMA (never in mitosis gene a)-related Kinase 6 (NEK6, Accession NM_014397) is another VGAM1064 host target gene. NEK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEK6 BINDING SITE, designated SEQ ID:15739, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39014] Another function of VGAM1064 is therefore inhibition of NIMA (never in mitosis gene a)-related Kinase 6 (NEK6, Accession NM_014397), a gene which regulates nuclear and cytoplasmic aspects of the mitotic cycle. Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEK6. The function of NEK6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM426.FLJ13397 (Accession NM_024948) is another VGAM1064 host target gene. FLJ13397 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by FLJ13397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13397 BINDING SITE, designated SEQ ID:24502, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39015] Another function of VGAM1064 is therefore inhibition of FLJ13397 (Accession NM_024948). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13397. KIAA0993 (Accession XM_034413) is another VGAM1064 host target gene. KIAA0993 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0993 BINDING SITE, designated SEQ ID:32077, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39016] Another function of VGAM1064 is therefore inhibition of KIAA0993 (Accession XM_034413). Accordingly, utilities

of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0993. Neuron Navigator 3 (NAV3, Accession NM_014903) is another VGAM1064 host target gene. NAV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAV3 BINDING SITE, designated SEQ ID:17089, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39017] Another function of VGAM1064 is therefore inhibition of Neuron Navigator 3 (NAV3, Accession NM_014903). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAV3. Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 2 (STAM2, Accession NM_005843) is another VGAM1064 host target gene. STAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of STAM2 BINDING SITE, designated SEQ ID:12457, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39018] Another function of VGAM1064 is therefore inhibition of Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 2 (STAM2, Accession NM_005843). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAM2. LOC146452 (Accession XM_085473) is another VGAM1064 host target gene. LOC146452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146452 BINDING SITE, designated SEQ ID:38163, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39019] Another function of VGAM1064 is therefore inhibition of LOC146452 (Accession XM_085473). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC146452. LOC149153 (Accession XM_097599) is another VGAM1064 host target gene. LOC149153 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149153 BINDING SITE, designated SEQ ID:40963, to the nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39020] Another function of VGAM1064 is therefore inhibition of LOC149153 (Accession XM_097599). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149153. LOC90750 (Accession XM_033868) is another VGAM1064 host target gene. LOC90750 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90750 BINDING SITE, designated SEQ ID:31964, to the

nucleotide sequence of VGAM1064 RNA, herein designated VGAM RNA, also designated SEQ ID:3775.

[39021] Another function of VGAM1064 is therefore inhibition of LOC90750 (Accession XM_033868). Accordingly, utilities of VGAM1064 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90750. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1065 (VGAM1065) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39022] VGAM1065 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1065 was detected is described hereinabove with reference to Figs. 1–8.

[39023] VGAM1065 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tulip Virus X.

VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39024] VGAM1065 gene encodes a VGAM1065 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1065 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1065 precursor RNA is designated SEQ ID:1051, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1051 is located at position 1206 relative to the genome of Tulip Virus X.

[39025] VGAM1065 precursor RNA folds onto itself, forming VGAM1065 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39026] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1065 folded precursor RNA into VGAM1065 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1065 RNA is designated SEQ ID:3776, and is provided hereinbelow with reference to the sequence listing part.

[39027] VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1065 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39028] VGAM1065 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1065 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1065 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39029] The complementary binding of VGAM1065 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1065 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1065 host target RNA into VGAM1065 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39030] It is appreciated that VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1065 host target genes. The mRNA of each one of this plurality of VGAM1065 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1065 RNA, herein designated VGAM RNA, and which when bound by VGAM1065 RNA causes inhibition of translation of respective one or more VGAM1065 host target proteins.

[39031] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1065 gene, herein designated VGAM GENE, on one or more VGAM1065 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[39032] It is yet further appreciated that a function of VGAM1065 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of viral infection by Tulip Virus X. Specific functions, and accordingly utilities, of VGAM1065 correlate with, and may be deduced from, the identity of the host target genes which VGAM1065 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39033] Nucleotide sequences of the VGAM1065 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1065 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1065 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1065 are further described hereinbelow with reference to Table 1.

[39034] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1065 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1065 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39035] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1065 gene, herein designated VGAM is inhibition of expression of VGAM1065 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1065 correlate with, and may be deduced from, the identity of the target genes which VGAM1065 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39036] Citron (rho-interacting, serine/threonine kinase 21) (CIT, Accession XM_045786) is a VGAM1065 host target gene. CIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIT BINDING SITE, designated SEQ ID:34560, to the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, also designated SEQ ID:3776.

[39037] A function of VGAM1065 is therefore inhibition of Citron (rho-interacting, serine/threonine kinase 21) (CIT, Acces-

sion XM_045786), a gene which is increased several-fold by coexpression of constitutively active Rho . Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIT. The function of CIT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM393. Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM_001418) is another VGAM1065 host target gene. EIF4G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4G2 BINDING SITE, designated SEQ ID:7115, to the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, also designated SEQ ID:3776.

[39038] Another function of VGAM1065 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM_001418), a gene which is a repressor of translation. Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with EIF4G2. The function of EIF4G2 has been established by previous studies. Imataka et al. (1997) used immunoprecipitation studies with HA- or FLAG-tagged proteins to show that p97 specifically binds to EIF4A and EIF3, but not to EIF4E (OMIM Ref. No. 133440) in vitro. Transient transfection experiments showed that p97 suppressed both cap-dependent and independent translation, and that overexpression of p97 reduced overall protein synthesis. Imataka et al. (1997) suggested that p97 is a general repressor of translation that acts by forming translationally inactive complexes. Levy-Strumpf et al. (1997) showed that while a fragment of DAP5 cDNA from the C-terminal region (encoding a 28-kD 'miniprotein') protected cells from IFNG-induced programmed cell death at low levels of expression, higher levels of expression were toxic. They proposed that the miniprotein may be a dominant-negative inhibitor of the essential DAP5 protein, and that DAP5 may play a specific role in apoptosis.

[39039] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39040] Imataka, H.; Olsen, H. S.; Sonenberg. N. : A new transla-

tional regulator with homology to eukaryotic translation initiation factor 4G. EMBO J. 16: 817–825, 1997. ; and

[39041] Levy–Strumpf, N.; Deiss, L. P.; Berissi, H.; Kimchi, A. : DAP–5, a novel homolog of eukaryotic translation initiation factor 4G isolated as a putative modulator of gamma interferon–indu.

[39042] Further studies establishing the function and utilities of EIF4G2 are found in John Hopkins OMIM database record ID 602325, and in cited publications numbered 6302–6303, 346 and 6304–6305 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Receptor Coactivator 4 (NCOA4, Accession NM_005437) is another VGAM1065 host target gene. NCOA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NCOA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA4 BINDING SITE, designated SEQ ID:11923, to the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, also designated SEQ ID:3776.

[39043] Another function of VGAM1065 is therefore inhibition of

Nuclear Receptor Coactivator 4 (NCOA4, Accession NM_005437), a gene which Binds and activates androgen receptor (AR) in ligand-dependent manner. Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA4. The function of NCOA4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM420.FLJ11850 (Accession NM_022741) is another VGAM1065 host target gene. FLJ11850 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11850, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11850 BINDING SITE, designated SEQ ID:22948, to the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, also designated SEQ ID:3776.

[39044] Another function of VGAM1065 is therefore inhibition of FLJ11850 (Accession NM_022741). Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ11850. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM1065 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7859, to the nucleotide sequence of VGAM1065 RNA, herein designated VGAM RNA, also designated SEQ ID:3776.

[39045] Another function of VGAM1065 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM1065 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1066 (VGAM1066) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39046] VGAM1066 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1066 was detected is described hereinabove with reference to Figs. 1–8.

[39047] VGAM1066 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tulip Virus X.

VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39048] VGAM1066 gene encodes a VGAM1066 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1066 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1066 precursor RNA is designated SEQ ID:1052, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1052 is located at position 2880 relative to the genome of Tulip Virus X.

[39049] VGAM1066 precursor RNA folds onto itself, forming VGAM1066 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39050] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1066 folded precursor RNA into VGAM1066 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1066 RNA is designated SEQ ID:3777, and is provided hereinbelow with reference to the sequence listing part.

[39051] VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1066 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39052] VGAM1066 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1066 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1066 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39053] The complementary binding of VGAM1066 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1066 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1066 host target RNA into VGAM1066 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39054] It is appreciated that VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1066 host target genes. The mRNA of each one of this plurality of VGAM1066 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1066 RNA, herein designated VGAM RNA, and which when bound by VGAM1066 RNA causes inhibition of translation of respective one or more VGAM1066 host target proteins.

[39055] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1066 gene, herein designated VGAM GENE, on one or more VGAM1066 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39056] It is yet further appreciated that a function of VGAM1066 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1066 include diagnosis, prevention and treatment of viral infection by Tulip Virus X. Specific functions, and accordingly utilities, of VGAM1066 correlate with, and may be deduced from, the identity of the host target genes which VGAM1066 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39057] Nucleotide sequences of the VGAM1066 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1066 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1066 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1066 are further described hereinbelow with reference to Table 1.

[39058] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1066 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1066 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39059] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1066 gene, herein designated VGAM is inhibition of expression of VGAM1066 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1066 correlate with, and may be deduced from, the identity of the target genes which VGAM1066 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39060] Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM_000322) is a VGAM1066 host target gene. RDS BINDING SITE is HOST TARGET binding site found in

the 5` untranslated region of mRNA encoded by RDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDS BINDING SITE, designated SEQ ID:5861, to the nucleotide sequence of VGAM1066 RNA, herein designated VGAM RNA, also designated SEQ ID:3777.

[39061] A function of VGAM1066 is therefore inhibition of Retinal Degeneration, Slow (retinitis pigmentosa 7) (RDS, Accession NM_000322), a gene which may function as an adhesion molecule involved in stabilization and compaction of outer segment disks or in the maintenance of the curvature of the rim. Accordingly, utilities of VGAM1066 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDS. The function of RDS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341.CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838) is another VGAM1066 host target gene. CSMD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSMD1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE, designated SEQ ID:36190, to the nucleotide sequence of VGAM1066 RNA, herein designated VGAM RNA, also designated SEQ ID:3777.

[39062] Another function of VGAM1066 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838). Accordingly, utilities of VGAM1066 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. GRWD (Accession NM_031485) is another VGAM1066 host target gene. GRWD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRWD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRWD BINDING SITE, designated SEQ ID:25575, to the nucleotide sequence of VGAM1066 RNA, herein designated VGAM RNA, also designated SEQ ID:3777.

[39063] Another function of VGAM1066 is therefore inhibition of GRWD (Accession NM_031485). Accordingly, utilities of

VGAM1066 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRWD. LOC257364 (Accession XM_170768) is another VGAM1066 host target gene. LOC257364 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257364 BINDING SITE, designated SEQ ID:45524, to the nucleotide sequence of VGAM1066 RNA, herein designated VGAM RNA, also designated SEQ ID:3777.

[39064] Another function of VGAM1066 is therefore inhibition of LOC257364 (Accession XM_170768). Accordingly, utilities of VGAM1066 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257364. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1067 (VGAM1067) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39065] VGAM1067 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1067 was detected is described hereinabove with reference to Figs. 1–8.

[39066] VGAM1067 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39067] VGAM1067 gene encodes a VGAM1067 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1067 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1067 precursor RNA is designated SEQ ID:1053, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1053 is located at position 2170 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39068] VGAM1067 precursor RNA folds onto itself, forming VGAM1067 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39069] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1067 folded precursor RNA into VGAM1067 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1067 RNA is designated SEQ ID:3778, and is provided hereinbelow with reference to the sequence listing part.

[39070] VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1067 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[39071] VGAM1067 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1067 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1067 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39072] The complementary binding of VGAM1067 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1067 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1067 host target RNA into VGAM1067 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39073] It is appreciated that VGAM1067 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1067 host target genes. The mRNA of each one of this plurality of VGAM1067 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1067 RNA, herein designated VGAM RNA, and which when bound by VGAM1067 RNA causes inhibition of translation of respective one or more VGAM1067 host target proteins.

[39074] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1067 gene, herein designated VGAM GENE, on one or more VGAM1067 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39075] It is yet further appreciated that a function of VGAM1067 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1067 correlate with, and may be deduced from, the identity of the host target genes which VGAM1067 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39076] Nucleotide sequences of the VGAM1067 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1067 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1067 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1067 are further
described hereinbelow with reference to Table 1.

[39077] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1067 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1067 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[39078] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1067 gene, herein designated VGAM is
inhibition of expression of VGAM1067 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1067 correlate with, and may be deduced
from, the identity of the target genes which VGAM1067
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[39079] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase,
Polypeptide 6 (B4GALT6, Accession XM_008799) is a

VGAM1067 host target gene. B4GALT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT6 BINDING SITE, designated SEQ ID:30094, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39080] A function of VGAM1067 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 6 (B4GALT6, Accession XM_008799). Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT6. CDC-like Kinase 2 (CLK2, Accession NM_001291) is another VGAM1067 host target gene. CLK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLK2 BINDING SITE, designated SEQ ID:6973, to the nucleotide sequence of VGAM1067 RNA, herein

designated VGAM RNA, also designated SEQ ID:3778.

[39081] Another function of VGAM1067 is therefore inhibition of CDC-like Kinase 2 (CLK2, Accession NM_001291), a gene which catalyzes the phosphorylation of proteins. Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLK2. The function of CLK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM356. Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083) is another VGAM1067 host target gene. CNR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNR1 BINDING SITE, designated SEQ ID:18164, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39082] Another function of VGAM1067 is therefore inhibition of Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083), a gene which is involved in the cannabi-

noid-induced CNS effects. Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNR1. The function of CNR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM533. Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293) is another VGAM1067 host target gene. LAMC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMC1 BINDING SITE, designated SEQ ID:8077, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39083] Another function of VGAM1067 is therefore inhibition of Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293), a gene which may mediate the attachment, migration, and organization of cells into tissues. Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with LAMC1. The function of LAMC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM812. KIAA1674 (Accession XM_044065) is another VGAM1067 host target gene.

KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34114, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39084] Another function of VGAM1067 is therefore inhibition of KIAA1674 (Accession XM_044065). Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. LOC147093 (Accession XM_097184) is another VGAM1067 host target gene. LOC147093 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147093, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147093 BINDING SITE, designated SEQ ID:40804, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39085] Another function of VGAM1067 is therefore inhibition of LOC147093 (Accession XM_097184). Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147093. LOC170395 (Accession XM_084325) is another VGAM1067 host target gene. LOC170395 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170395 BINDING SITE, designated SEQ ID:37546, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39086] Another function of VGAM1067 is therefore inhibition of LOC170395 (Accession XM_084325). Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC170395. LOC200609 (Accession XM_117256) is another VGAM1067 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43331, to the nucleotide sequence of VGAM1067 RNA, herein designated VGAM RNA, also designated SEQ ID:3778.

[39087] Another function of VGAM1067 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM1067 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1068 (VGAM1068) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39088] VGAM1068 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1068 was detected is described hereinabove with reference to Figs. 1–8.

[39089] VGAM1068 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39090] VGAM1068 gene encodes a VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1068 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1068 precursor RNA is designated SEQ ID:1054, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1054 is located at position 12381 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39091] VGAM1068 precursor RNA folds onto itself, forming VGAM1068 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39092] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1068 folded precursor RNA into VGAM1068 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1068 RNA is designated SEQ ID:3779, and is provided hereinbelow with reference to the sequence listing part.

[39093] VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1068 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39094] VGAM1068 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1068 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1068 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[39095] The complementary binding of VGAM1068 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1068 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1068 host target RNA into VGAM1068 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39096] It is appreciated that VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1068 host target genes. The mRNA of each one of this plurality of VGAM1068 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1068 RNA, herein designated VGAM RNA, and which when bound by VGAM1068 RNA causes inhibition of translation of respective one or more VGAM1068 host target proteins.

[39097] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1068 gene, herein designated VGAM GENE, on one or more VGAM1068 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39098] It is yet further appreciated that a function of VGAM1068 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1068 correlate with, and may be deduced from, the identity of the host target genes which VGAM1068 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39099] Nucleotide sequences of the VGAM1068 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1068 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1068 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1068 are further described hereinbelow with reference to Table 1.

[39100] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1068 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1068 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39101] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1068 gene, herein designated VGAM is inhibition of expression of VGAM1068 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1068 correlate with, and may be deduced from, the identity of the target genes which VGAM1068 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39102] Nuclear Receptor Subfamily 5, Group A, Member 2 (NR5A2, Accession NM_003822) is a VGAM1068 host target gene. NR5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by NR5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR5A2 BINDING SITE, designated SEQ ID:9914, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39103] A function of VGAM1068 is therefore inhibition of Nuclear Receptor Subfamily 5, Group A, Member 2 (NR5A2, Accession NM_003822), a gene which is a member of nuclear receptor superfamily of transcriptional activators and activates the hepatitis B virus (HBV) promoter. Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR5A2. The function of NR5A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM375. Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198) is another VGAM1068 host target gene. PDK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK4 BINDING SITE, designated SEQ ID:46443, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39104] Another function of VGAM1068 is therefore inhibition of Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK4. Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM_002646) is another VGAM1068 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3C2B BINDING SITE, designated SEQ ID:8504, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39105] Another function of VGAM1068 is therefore inhibition of Phosphoinositide-3-kinase, Class 2, Beta Polypeptide

(PIK3C2B, Accession NM_002646). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961) is another VGAM1068 host target gene. PTGIS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGIS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGIS BINDING SITE, designated SEQ ID:6665, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39106] Another function of VGAM1068 is therefore inhibition of Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961), a gene which catalyzes the isomerization of prostaglandin h₂ to prostacyclin (= prostaglandin i₂). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGIS. The function of PTGIS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Bromodomain Con-

taining 3 (BRD3, Accession NM_007371) is another VGAM1068 host target gene. BRD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRD3 BINDING SITE, designated SEQ ID:14296, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39107] Another function of VGAM1068 is therefore inhibition of Bromodomain Containing 3 (BRD3, Accession NM_007371). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD3. Cyclin E2 (CCNE2, Accession NM_057749) is another VGAM1068 host target gene. CCNE2 BINDING SITE1 and CCNE2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCNE2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNE2 BINDING SITE1 and CCNE2 BINDING SITE2, designated SEQ

ID:27710 and SEQ ID:11049 respectively, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39108] Another function of VGAM1068 is therefore inhibition of Cyclin E2 (CCNE2, Accession NM_057749). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNE2. KIAA0475 (Accession NM_014864) is another VGAM1068 host target gene. KIAA0475 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0475 BINDING SITE, designated SEQ ID:16950, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39109] Another function of VGAM1068 is therefore inhibition of KIAA0475 (Accession NM_014864). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0475. KIAA0931 (Accession XM_041191) is another VGAM1068 host target gene. KIAA0931 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0931 BINDING SITE, designated SEQ ID:33486, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39110] Another function of VGAM1068 is therefore inhibition of KIAA0931 (Accession XM_041191). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0931. Protocadherin 17 (PCDH17, Accession NM_014459) is another VGAM1068 host target gene. PCDH17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH17 BINDING SITE, designated SEQ ID:15810, to the nucleotide sequence of VGAM1068 RNA, herein designated VGAM RNA, also designated SEQ ID:3779.

[39111] Another function of VGAM1068 is therefore inhibition of Protocadherin 17 (PCDH17, Accession NM_014459). Accordingly, utilities of VGAM1068 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH17. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1069 (VGAM1069) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39112] VGAM1069 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1069 was detected is described hereinabove with reference to Figs. 1–8.

[39113] VGAM1069 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39114] VGAM1069 gene encodes a VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1069 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1069 precursor RNA is designated SEQ ID:1055, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1055 is located at position 4727 relative to the genome of Porcine Epidemic Diarrhea Virus.

- [39115] VGAM1069 precursor RNA folds onto itself, forming VGAM1069 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39116] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1069 folded precursor RNA into VGAM1069 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1069 RNA is designated SEQ ID:3780, and is provided hereinbelow with reference to the sequence listing part.

[39117] VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1069 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39118] VGAM1069 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1069 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1069 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39119] The complementary binding of VGAM1069 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1069 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1069 host target RNA into VGAM1069 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39120] It is appreciated that VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1069 host target genes. The mRNA of each one of this plurality of VGAM1069 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1069 RNA, herein designated VGAM RNA, and which when bound by VGAM1069 RNA causes inhibition of translation of respective one or more VGAM1069 host target proteins.

[39121] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1069 gene, herein designated VGAM GENE, on one or more VGAM1069 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39122] It is yet further appreciated that a function of VGAM1069 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1069 correlate with, and may be deduced from, the identity of the host target genes which VGAM1069 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39123] Nucleotide sequences of the VGAM1069 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1069 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1069 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1069 are further described hereinbelow with reference to Table 1.

[39124] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1069 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1069 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[39125] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1069 gene, herein designated VGAM is inhibition of expression of VGAM1069 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1069 correlate with, and may be deduced from, the identity of the target genes which VGAM1069 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39126] A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis factor, alpha, converting enzyme) (ADAM17, Accession NM_021832) is a VGAM1069 host target gene. ADAM17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM17 BINDING SITE, designated SEQ ID:22407, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39127] A function of VGAM1069 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis

factor, alpha, converting enzyme) (ADAM17, Accession NM_021832), a gene which member of ADAM family of zinc metalloproteases. Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM17. The function of ADAM17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Cadherin 3, Type 1, P-cadherin (placental) (CDH3, Accession NM_001793) is another VGAM1069 host target gene. CDH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH3 BINDING SITE, designated SEQ ID:7544, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39128] Another function of VGAM1069 is therefore inhibition of Cadherin 3, Type 1, P-cadherin (placental) (CDH3, Accession NM_001793), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM1069

include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH3. The function of CDH3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662) is another VGAM1069 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19193, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39129] Another function of VGAM1069 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of

TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.CAMP-GEFII (Accession NM_007023) is another VGAM1069 host target gene. CAMP-GEFII BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMP-GEFII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMP-GEFII BINDING SITE, designated SEQ ID:13878, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39130] Another function of VGAM1069 is therefore inhibition of CAMP-GEFII (Accession NM_007023). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMP-GEFII. FLJ11827 (Accession NM_025093) is another VGAM1069 host target gene. FLJ11827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ11827 BINDING SITE, designated SEQ ID:24724, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39131] Another function of VGAM1069 is therefore inhibition of FLJ11827 (Accession NM_025093). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11827. FLJ20035 (Accession NM_017631) is another VGAM1069 host target gene. FLJ20035 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20035 BINDING SITE, designated SEQ ID:19139, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39132] Another function of VGAM1069 is therefore inhibition of FLJ20035 (Accession NM_017631). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20035. KIAA0319 (Accession NM_014809) is another

VGAM1069 host target gene. KIAA0319 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0319 BINDING SITE, designated SEQ ID:16759, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39133] Another function of VGAM1069 is therefore inhibition of KIAA0319 (Accession NM_014809). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0319. KIAA0630 (Accession XM_114729) is another VGAM1069 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43060, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39134] Another function of VGAM1069 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. KIAA0924 (Accession NM_014897) is another VGAM1069 host target gene. KIAA0924 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0924 BINDING SITE, designated SEQ ID:17063, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39135] Another function of VGAM1069 is therefore inhibition of KIAA0924 (Accession NM_014897). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0924. YKT6 (Accession NM_006555) is another VGAM1069 host target gene. YKT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YKT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YKT6 BINDING SITE, designated SEQ ID:13320, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39136] Another function of VGAM1069 is therefore inhibition of YKT6 (Accession NM_006555). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YKT6. LOC148413 (Accession XM_086176) is another VGAM1069 host target gene. LOC148413 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148413 BINDING SITE, designated SEQ ID:38531, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39137] Another function of VGAM1069 is therefore inhibition of LOC148413 (Accession XM_086176). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC148413. LOC150225 (Accession XM_097870) is another VGAM1069 host target gene. LOC150225 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150225 BINDING SITE, designated SEQ ID:41188, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39138] Another function of VGAM1069 is therefore inhibition of LOC150225 (Accession XM_097870). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150225. LOC91812 (Accession XM_040857) is another VGAM1069 host target gene. LOC91812 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91812 BINDING SITE, designated SEQ ID:33390, to the nucleotide sequence of VGAM1069 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3780.

[39139] Another function of VGAM1069 is therefore inhibition of LOC91812 (Accession XM_040857). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91812. LOC91813 (Accession XM_040862) is another VGAM1069 host target gene. LOC91813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE, designated SEQ ID:33396, to the nucleotide sequence of VGAM1069 RNA, herein designated VGAM RNA, also designated SEQ ID:3780.

[39140] Another function of VGAM1069 is therefore inhibition of LOC91813 (Accession XM_040862). Accordingly, utilities of VGAM1069 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1070 (VGAM1070) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39141] VGAM1070 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1070 was detected is described hereinabove with reference to Figs. 1–8.

[39142] VGAM1070 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39143] VGAM1070 gene encodes a VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1070 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1070 precursor RNA is designated SEQ ID:1056, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1056 is located at position 6437 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39144] VGAM1070 precursor RNA folds onto itself, forming

VGAM1070 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39145] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1070 folded precursor RNA into VGAM1070 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1070 RNA is designated SEQ ID:3781, and is provided hereinbelow with reference to the sequence listing part.

[39146] VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1070 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[39147] VGAM1070 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1070 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1070 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39148] The complementary binding of VGAM1070 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1070 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1070 host target RNA into VGAM1070 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39149] It is appreciated that VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1070 host target genes. The mRNA of each one of this plurality of VGAM1070 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1070 RNA, herein designated VGAM RNA, and which when bound by VGAM1070 RNA causes inhibition of translation of respective one or more VGAM1070 host target proteins.

[39150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1070 gene, herein designated VGAM GENE, on one or more VGAM1070 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39151] It is yet further appreciated that a function of VGAM1070 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1070 correlate with, and may be deduced from, the identity of the host target genes which VGAM1070 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39152] Nucleotide sequences of the VGAM1070 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1070 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1070 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1070 are further described hereinbelow with reference to Table 1.

[39153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1070 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1070 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39154] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1070 gene, herein designated VGAM is inhibition of expression of VGAM1070 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1070 correlate with, and may be deduced from, the identity of the target genes which VGAM1070 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[39155] Angiopoietin 1 (ANGPT1, Accession NM_001146) is a VGAM1070 host target gene. ANGPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANGPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANGPT1 BINDING SITE, designated SEQ ID:6812, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39156] A function of VGAM1070 is therefore inhibition of Angiopoietin 1 (ANGPT1, Accession NM_001146), a gene which binds and activates tie2 receptor by inducing its tyrosine phosphorylation. Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANGPT1. The function of ANGPT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM291. Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487) is another VGAM1070 host target gene. CDKN2B BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDKN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2B BINDING SITE, designated SEQ ID:27806, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39157] Another function of VGAM1070 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2B. ATIP1 (Accession NM_020749) is another VGAM1070 host target gene. ATIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATIP1 BINDING SITE, designated SEQ ID:21862, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39158] Another function of VGAM1070 is therefore inhibition of ATIP1 (Accession NM_020749). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATIP1. FLJ11273 (Accession NM_018374) is another VGAM1070 host target gene. FLJ11273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11273 BINDING SITE, designated SEQ ID:20395, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39159] Another function of VGAM1070 is therefore inhibition of FLJ11273 (Accession NM_018374). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11273. FLJ20716 (Accession NM_017938) is another VGAM1070 host target gene. FLJ20716 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20716 BINDING SITE, designated SEQ ID:19630, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39160] Another function of VGAM1070 is therefore inhibition of FLJ20716 (Accession NM_017938). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20716. MGC13138 (Accession NM_033410) is another VGAM1070 host target gene. MGC13138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13138 BINDING SITE, designated SEQ ID:27230, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39161] Another function of VGAM1070 is therefore inhibition of MGC13138 (Accession NM_033410). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC13138. QKI (Accession XM_037438) is another VGAM1070 host target gene. QKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by QKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of QKI BINDING SITE, designated SEQ ID:32616, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39162] Another function of VGAM1070 is therefore inhibition of QKI (Accession XM_037438). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with QKI. LOC148188 (Accession XM_086088) is another VGAM1070 host target gene. LOC148188 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148188, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148188 BINDING SITE, designated SEQ ID:38489, to the nucleotide sequence of VGAM1070 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3781.

[39163] Another function of VGAM1070 is therefore inhibition of LOC148188 (Accession XM_086088). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148188. LOC201522 (Accession XM_113978) is another VGAM1070 host target gene. LOC201522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201522 BINDING SITE, designated SEQ ID:42585, to the nucleotide sequence of VGAM1070 RNA, herein designated VGAM RNA, also designated SEQ ID:3781.

[39164] Another function of VGAM1070 is therefore inhibition of LOC201522 (Accession XM_113978). Accordingly, utilities of VGAM1070 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201522. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1071 (VGAM1071) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39165] VGAM1071 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1071 was detected is described hereinabove with reference to Figs. 1–8.

[39166] VGAM1071 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39167] VGAM1071 gene encodes a VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1071 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1071 precursor RNA is designated SEQ ID:1057, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1057 is located at position 5412 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39168] VGAM1071 precursor RNA folds onto itself, forming

VGAM1071 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39169] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1071 folded precursor RNA into VGAM1071 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1071 RNA is designated SEQ ID:3782, and is provided hereinbelow with reference to the sequence listing part.

[39170] VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1071 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[39171] VGAM1071 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1071 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1071 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39172] The complementary binding of VGAM1071 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1071 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1071 host target RNA into VGAM1071 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39173] It is appreciated that VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1071 host target genes. The mRNA of each one of this plurality of VGAM1071 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1071 RNA, herein designated VGAM RNA, and which when bound by VGAM1071 RNA causes inhibition of translation of respective one or more VGAM1071 host target proteins.

[39174] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1071 gene, herein designated VGAM GENE, on one or more VGAM1071 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39175] It is yet further appreciated that a function of VGAM1071 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1071 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1071 correlate with, and may be deduced from, the identity of the host target genes which VGAM1071 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39176] Nucleotide sequences of the VGAM1071 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1071 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1071 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1071 are further described hereinbelow with reference to Table 1.

[39177] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1071 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1071 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39178] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1071 gene, herein designated VGAM is inhibition of expression of VGAM1071 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1071 correlate with, and may be deduced from, the identity of the target genes which VGAM1071 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[39179] Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823) is a VGAM1071 host target gene. PKIA BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PKIA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIA BINDING SITE, designated SEQ ID:13696, to the nucleotide sequence of VGAM1071 RNA, herein designated VGAM RNA, also designated SEQ ID:3782.

[39180] A function of VGAM1071 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823). Accordingly, utilities of VGAM1071 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIA. LOC253260 (Accession XM_171097) is another VGAM1071 host target gene. LOC253260 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC253260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC253260 BINDING SITE, designated SEQ ID:45908, to the nucleotide sequence of VGAM1071 RNA, herein designated VGAM RNA, also designated SEQ ID:3782.

[39181] Another function of VGAM1071 is therefore inhibition of LOC253260 (Accession XM_171097). Accordingly, utilities of VGAM1071 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253260. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1072 (VGAM1072) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39182] VGAM1072 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1072 was detected is described hereinabove with reference to Figs. 1–8.

[39183] VGAM1072 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39184] VGAM1072 gene encodes a VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1072 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1072 precursor RNA is designated SEQ ID:1058, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1058 is located at position 10299 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39185] VGAM1072 precursor RNA folds onto itself, forming VGAM1072 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39186] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1072 folded precursor RNA into VGAM1072 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1072 RNA is designated SEQ ID:3783, and is provided hereinbelow with reference to the sequence listing part.

[39187] VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1072 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39188] VGAM1072 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1072 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1072 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39189] The complementary binding of VGAM1072 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1072 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1072 host target RNA into VGAM1072 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39190] It is appreciated that VGAM1072 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1072 host target genes. The mRNA of each one of this plurality of VGAM1072 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1072 RNA, herein designated VGAM RNA, and which when bound by VGAM1072 RNA causes inhibition of translation of respective one or more VGAM1072 host target proteins.

[39191] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1072 gene, herein designated VGAM GENE, on one or more VGAM1072 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[39192] It is yet further appreciated that a function of VGAM1072 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1072 correlate with, and may be deduced from, the identity of the host target genes which VGAM1072 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39193] Nucleotide sequences of the VGAM1072 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1072 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1072 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1072 are further described hereinbelow with reference to Table 1.

[39194] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1072 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1072 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39195] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1072 gene, herein designated VGAM is inhibition of expression of VGAM1072 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1072 correlate with, and may be deduced from, the identity of the target genes which VGAM1072 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39196] Sialic Acid Binding Ig-like Lectin 11 (SIGLEC11, Accession NM_052884) is a VGAM1072 host target gene. SIGLEC11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIGLEC11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIGLEC11 BINDING SITE, designated SEQ ID:27463, to the nucleotide sequence of VGAM1072 RNA, herein designated VGAM RNA, also designated SEQ ID:3783.

[39197] A function of VGAM1072 is therefore inhibition of Sialic Acid Binding Ig-like Lectin 11 (SIGLEC11, Accession NM_052884). Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIGLEC11. KIAA0977 (Accession NM_014900) is another VGAM1072 host target gene. KIAA0977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0977 BINDING SITE, designated SEQ ID:17081, to the nucleotide sequence of VGAM1072 RNA, herein designated VGAM RNA, also designated SEQ ID:3783.

[39198] Another function of VGAM1072 is therefore inhibition of KIAA0977 (Accession NM_014900). Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0977. SEC24 Related Gene Family, Member A (*S. cerevisiae*) (SEC24A, Accession XM_094581) is another VGAM1072 host target gene. SEC24A BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SEC24A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC24A BINDING SITE, designated SEQ ID:40236, to the nucleotide sequence of VGAM1072 RNA, herein designated VGAM RNA, also designated SEQ ID:3783.

[39199] Another function of VGAM1072 is therefore inhibition of SEC24 Related Gene Family, Member A (*S. cerevisiae*) (SEC24A, Accession XM_094581). Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC24A. LOC146050 (Accession XM_085301) is another VGAM1072 host target gene. LOC146050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146050 BINDING SITE, designated SEQ ID:38054, to the nucleotide sequence of VGAM1072 RNA, herein designated VGAM RNA, also designated SEQ ID:3783.

[39200] Another function of VGAM1072 is therefore inhibition of

LOC146050 (Accession XM_085301). Accordingly, utilities of VGAM1072 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1073 (VGAM1073) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39201] VGAM1073 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1073 was detected is described hereinabove with reference to Figs. 1-8.

[39202] VGAM1073 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39203] VGAM1073 gene encodes a VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1073 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1073 precursor RNA is designated SEQ ID:1059, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1059 is located at position 11550 relative to the genome of Porcine Epidemic Diarrhea Virus.

- [39204] VGAM1073 precursor RNA folds onto itself, forming VGAM1073 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39205] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1073 folded precursor RNA into VGAM1073 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM1073 RNA is designated SEQ ID:3784, and is provided hereinbelow with reference to the sequence listing part.

[39206] VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1073 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39207] VGAM1073 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1073 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1073 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[39208] The complementary binding of VGAM1073 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1073 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1073 host target RNA into VGAM1073 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39209] It is appreciated that VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1073 host target genes. The mRNA of each one of this plurality of VGAM1073 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1073 RNA, herein designated VGAM RNA, and which when bound by VGAM1073 RNA causes inhibition of translation of respective one or more VGAM1073 host target proteins.

[39210] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1073 gene, herein designated VGAM GENE, on one or more VGAM1073 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39211] It is yet further appreciated that a function of VGAM1073

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1073 correlate with, and may be deduced from, the identity of the host target genes which VGAM1073 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39212] Nucleotide sequences of the VGAM1073 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1073 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1073 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1073 are further described hereinbelow with reference to Table 1.

[39213] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1073 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1073 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39214] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1073 gene, herein designated VGAM is inhibition of expression of VGAM1073 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1073 correlate with, and may be deduced from, the identity of the target genes which VGAM1073 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39215] Lipase, Member I (LIPI, Accession XM_086767) is a VGAM1073 host target gene. LIPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPI BINDING SITE, designated SEQ ID:38843, to the nucleotide sequence of VGAM1073 RNA, herein designated VGAM RNA, also designated SEQ ID:3784.

[39216] A function of VGAM1073 is therefore inhibition of Lipase, Member I (LIPI, Accession XM_086767). Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPI. PRO0902 (Accession NM_053057) is another

VGAM1073 host target gene. PRO0902 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO0902, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0902 BINDING SITE, designated SEQ ID:27607, to the nucleotide sequence of VGAM1073 RNA, herein designated VGAM RNA, also designated SEQ ID:3784.

[39217] Another function of VGAM1073 is therefore inhibition of PRO0902 (Accession NM_053057). Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0902. LOC153937 (Accession XM_087813) is another VGAM1073 host target gene. LOC153937 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39445, to the nucleotide sequence of VGAM1073 RNA, herein designated VGAM RNA, also designated SEQ ID:3784.

[39218] Another function of VGAM1073 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153937. LOC51028 (Accession NM_016075) is another VGAM1073 host target gene. LOC51028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51028 BINDING SITE, designated SEQ ID:18149, to the nucleotide sequence of VGAM1073 RNA, herein designated VGAM RNA, also designated SEQ ID:3784.

[39219] Another function of VGAM1073 is therefore inhibition of LOC51028 (Accession NM_016075). Accordingly, utilities of VGAM1073 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51028. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1074 (VGAM1074) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[39220] VGAM1074 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1074 was detected is described hereinabove with reference to Figs. 1-8.

[39221] VGAM1074 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39222] VGAM1074 gene encodes a VGAM1074 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1074 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1074 precursor RNA is designated SEQ ID:1060, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1060 is located at position 2902 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39223] VGAM1074 precursor RNA folds onto itself, forming VGAM1074 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39224] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1074 folded precursor RNA into VGAM1074 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1074 RNA is designated SEQ ID:3785, and is provided hereinbelow with reference to the sequence listing part.

[39225] VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1074 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39226] VGAM1074 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1074 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1074 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39227] The complementary binding of VGAM1074 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1074 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1074 host target RNA into VGAM1074 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39228] It is appreciated that VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1074 host target genes. The mRNA of each one of this plurality of VGAM1074 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1074 RNA, herein designated VGAM RNA, and which when bound by VGAM1074 RNA causes inhibition of translation of respective one or more VGAM1074 host target proteins.

[39229] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1074 gene, herein designated VGAM GENE, on one or more VGAM1074 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39230] It is yet further appreciated that a function of VGAM1074 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1074 correlate with, and may be deduced from, the identity of the host target genes which VGAM1074 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[39231] Nucleotide sequences of the VGAM1074 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1074 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1074 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1074 are further described hereinbelow with reference to Table 1.

[39232] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1074 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1074 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39233] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1074 gene, herein designated VGAM is inhibition of expression of VGAM1074 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1074 correlate with, and may be deduced from, the identity of the target genes which VGAM1074 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39234] Fibroblast Growth Factor Receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2, Accession NM_023030) is a VGAM1074 host target gene. FGFR2 BINDING SITE1 through FGFR2 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR2 BINDING SITE1 through FGFR2 BINDING SITE6, designated SEQ ID:23296, SEQ ID:23290, SEQ ID:23236, SEQ ID:23302, SEQ ID:5640 and SEQ ID:23243 respectively, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39235] A function of VGAM1074 is therefore inhibition of Fibroblast Growth Factor Receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2, Accession NM_023030). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with FGFR2. T-cell Leukemia Translocation Altered Gene (TCTA, Accession NM_022171) is another VGAM1074 host target gene. TCTA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCTA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCTA BINDING SITE, designated SEQ ID:22728, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39236] Another function of VGAM1074 is therefore inhibition of T-cell Leukemia Translocation Altered Gene (TCTA, Accession NM_022171). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCTA. Abhydrolase Domain Containing 3 (ABHD3, Accession NM_138340) is another VGAM1074 host target gene. ABHD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABHD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

ABHD3 BINDING SITE, designated SEQ ID:28740, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39237] Another function of VGAM1074 is therefore inhibition of Abhydrolase Domain Containing 3 (ABHD3, Accession NM_138340). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABHD3. FLJ10781 (Accession NM_018215) is another VGAM1074 host target gene. FLJ10781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10781 BINDING SITE, designated SEQ ID:20137, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39238] Another function of VGAM1074 is therefore inhibition of FLJ10781 (Accession NM_018215). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10781. FLJ31737 (Accession NM_144984) is another

VGAM1074 host target gene. FLJ31737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31737 BINDING SITE, designated SEQ ID:29591, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39239] Another function of VGAM1074 is therefore inhibition of FLJ31737 (Accession NM_144984). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31737. Hepatitis B Virus X Associated Protein (HBXAP, Accession NM_016578) is another VGAM1074 host target gene. HBXAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HBXAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HBXAP BINDING SITE, designated SEQ ID:18655, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ

ID:3785.

[39240] Another function of VGAM1074 is therefore inhibition of Hepatitis B Virus X Associated Protein (HBXAP, Accession NM_016578). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HBXAP. MEGF10 (Accession NM_032446) is another VGAM1074 host target gene. MEGF10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MEGF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF10 BINDING SITE, designated SEQ ID:26210, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39241] Another function of VGAM1074 is therefore inhibition of MEGF10 (Accession NM_032446). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEGF10. LOC219333 (Accession XM_167944) is another VGAM1074 host target gene. LOC219333 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by LOC219333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219333 BINDING SITE, designated SEQ ID:44932, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39242] Another function of VGAM1074 is therefore inhibition of LOC219333 (Accession XM_167944). Accordingly, utilities of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219333. LOC221405 (Accession XM_168138) is another VGAM1074 host target gene. LOC221405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221405 BINDING SITE, designated SEQ ID:45066, to the nucleotide sequence of VGAM1074 RNA, herein designated VGAM RNA, also designated SEQ ID:3785.

[39243] Another function of VGAM1074 is therefore inhibition of LOC221405 (Accession XM_168138). Accordingly, utilities

of VGAM1074 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221405. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1075 (VGAM1075) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39244] VGAM1075 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1075 was detected is described hereinabove with reference to Figs. 1-8.

[39245] VGAM1075 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39246] VGAM1075 gene encodes a VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1075 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1075 precursor RNA is designated SEQ ID:1061, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1061 is located at position 17939 relative to the genome of Porcine Epidemic Diarrhea Virus.

- [39247] VGAM1075 precursor RNA folds onto itself, forming VGAM1075 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39248] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1075 folded precursor RNA into VGAM1075 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1075 RNA is designated SEQ ID:3786, and

is provided hereinbelow with reference to the sequence listing part.

[39249] VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1075 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[39250] VGAM1075 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1075 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1075 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39251] The complementary binding of VGAM1075 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1075 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1075 host target RNA into VGAM1075 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39252] It is appreciated that VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1075 host target genes. The mRNA of each one of this plurality of VGAM1075 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1075 RNA, herein designated VGAM RNA, and which when bound by VGAM1075 RNA causes inhibition of translation of respective one or more VGAM1075 host target proteins.

[39253] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1075 gene, herein designated VGAM GENE, on one or more VGAM1075 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39254] It is yet further appreciated that a function of VGAM1075 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1075 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1075 correlate with, and may be deduced from, the identity of the host target genes which VGAM1075 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39255] Nucleotide sequences of the VGAM1075 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1075 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1075 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1075 are further described hereinbelow with reference to Table 1.

[39256] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1075 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1075 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39257] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1075 gene, herein designated VGAM is inhibition of expression of VGAM1075 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1075 correlate with, and may be deduced from, the identity of the target genes which VGAM1075 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39258] KIAA0630 (Accession XM_114729) is a VGAM1075 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43062, to the nucleotide sequence of VGAM1075 RNA, herein designated VGAM RNA, also designated SEQ ID:3786.

[39259] A function of VGAM1075 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM1075 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1076 (VGAM1076) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39260] VGAM1076 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1076 was detected is described hereinabove with reference to Figs. 1–8.

[39261] VGAM1076 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39262] VGAM1076 gene encodes a VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1076 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1076 precursor RNA is designated SEQ ID:1062, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1062 is located at position 17488 relative to the

genome of Porcine Epidemic Diarrhea Virus.

[39263] VGAM1076 precursor RNA folds onto itself, forming VGAM1076 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39264] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1076 folded precursor RNA into VGAM1076 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1076 RNA is designated SEQ ID:3787, and is provided hereinbelow with reference to the sequence listing part.

[39265] VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1076 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39266] VGAM1076 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1076 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1076 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39267] The complementary binding of VGAM1076 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1076 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1076 host target RNA into VGAM1076 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39268] It is appreciated that VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1076 host target genes. The mRNA of each one of this plurality of VGAM1076 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1076 RNA, herein designated VGAM RNA, and which when bound by VGAM1076 RNA causes inhibition of translation of respective one or more VGAM1076 host target proteins.

[39269] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1076 gene, herein designated VGAM GENE, on one or more VGAM1076 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39270] It is yet further appreciated that a function of VGAM1076 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of

VGAM1076 correlate with, and may be deduced from, the identity of the host target genes which VGAM1076 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39271] Nucleotide sequences of the VGAM1076 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1076 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1076 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1076 are further described hereinbelow with reference to Table 1.

[39272] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1076 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1076 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39273] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1076 gene, herein designated VGAM is inhibition of expression of VGAM1076 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1076 correlate with, and may be deduced

from, the identity of the target genes which VGAM1076 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39274] Indolethylamine N-methyltransferase (INMT, Accession NM_006774) is a VGAM1076 host target gene. INMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INMT BINDING SITE, designated SEQ ID:13648, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39275] A function of VGAM1076 is therefore inhibition of Indolethylamine N-methyltransferase (INMT, Accession NM_006774). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INMT. SRGAP1 (Accession XM_051143) is another VGAM1076 host target gene. SRGAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRGAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of SRGAP1 BINDING SITE, designated SEQ ID:35758, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39276] Another function of VGAM1076 is therefore inhibition of SRGAP1 (Accession XM_051143). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRGAP1. Von Hippel–Lindau Syndrome (VHL, Accession NM_000551) is another VGAM1076 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6157, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39277] Another function of VGAM1076 is therefore inhibition of Von Hippel–Lindau Syndrome (VHL, Accession NM_000551), a gene which may control rna stability through the selective degradation of rna-bound proteins.

Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM197. DKFZP566F2124 (Accession NM_015630) is another VGAM1076 host target gene. DKFZP566F2124 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566F2124, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566F2124 BINDING SITE, designated SEQ ID:17891, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39278] Another function of VGAM1076 is therefore inhibition of DKFZP566F2124 (Accession NM_015630). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566F2124. FLJ13910 (Accession NM_022780) is another VGAM1076 host target gene. FLJ13910 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by FLJ13910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13910 BINDING SITE, designated SEQ ID:23052, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39279] Another function of VGAM1076 is therefore inhibition of FLJ13910 (Accession NM_022780). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13910. FLJ22679 (Accession NM_017698) is another VGAM1076 host target gene. FLJ22679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22679 BINDING SITE, designated SEQ ID:19265, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39280] Another function of VGAM1076 is therefore inhibition of FLJ22679 (Accession NM_017698). Accordingly, utilities of

VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22679. Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007) is another VGAM1076 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLAGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34879, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39281] Another function of VGAM1076 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM_027679) is another VGAM1076 host target gene. RHOBTB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RHOBTB2, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB2 BINDING SITE, designated SEQ ID:30561, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39282] Another function of VGAM1076 is therefore inhibition of Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM_027679). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB2. UCK1 (Accession NM_031432) is another VGAM1076 host target gene. UCK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UCK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UCK1 BINDING SITE, designated SEQ ID:25427, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39283] Another function of VGAM1076 is therefore inhibition of UCK1 (Accession NM_031432). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UCK1.

LOC149465 (Accession XM_086543) is another VGAM1076 host target gene. LOC149465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149465 BINDING SITE, designated SEQ ID:38758, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39284] Another function of VGAM1076 is therefore inhibition of LOC149465 (Accession XM_086543). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149465. LOC199858 (Accession XM_114040) is another VGAM1076 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42641, to the nucleotide sequence of VGAM1076 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3787.

[39285] Another function of VGAM1076 is therefore inhibition of LOC199858 (Accession XM_114040). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC201182 (Accession XM_117055) is another VGAM1076 host target gene. LOC201182 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201182 BINDING SITE, designated SEQ ID:43210, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39286] Another function of VGAM1076 is therefore inhibition of LOC201182 (Accession XM_117055). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201182. LOC91050 (Accession XM_035703) is another VGAM1076 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32331, to the nucleotide sequence of VGAM1076 RNA, herein designated VGAM RNA, also designated SEQ ID:3787.

[39287] Another function of VGAM1076 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities of VGAM1076 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1077 (VGAM1077) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39288] VGAM1077 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1077 was detected is described hereinabove with reference to Figs. 1-8.

[39289] VGAM1077 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diar-

rhea Virus. VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39290] VGAM1077 gene encodes a VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1077 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1077 precursor RNA is designated SEQ ID:1063, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1063 is located at position 1109 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39291] VGAM1077 precursor RNA folds onto itself, forming VGAM1077 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39292] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1077 folded precursor RNA into VGAM1077 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1077 RNA is designated SEQ ID:3788, and is provided hereinbelow with reference to the sequence listing part.

[39293] VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1077 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39294] VGAM1077 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1077 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1077 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39295] The complementary binding of VGAM1077 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1077 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1077 host target RNA into VGAM1077 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39296] It is appreciated that VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1077 host target genes. The mRNA of each one of this plurality of VGAM1077 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1077 RNA, herein designated VGAM RNA, and which when bound by VGAM1077 RNA causes inhibition of translation of respective one or more VGAM1077 host target proteins.

[39297] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1077 gene, herein designated VGAM GENE, on one or more VGAM1077 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39298] It is yet further appreciated that a function of VGAM1077 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1077 correlate with, and may be deduced from, the identity of the host target genes which VGAM1077 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39299] Nucleotide sequences of the VGAM1077 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1077 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1077 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1077 are further described hereinbelow with reference to Table 1.

[39300] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1077 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1077 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39301] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1077 gene, herein designated VGAM is inhibition of expression of VGAM1077 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1077 correlate with, and may be deduced from, the identity of the target genes which VGAM1077 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39302] KIAA0618 (Accession NM_014833) is a VGAM1077 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16832, to the nucleotide sequence of

VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39303] A function of VGAM1077 is therefore inhibition of KIAA0618 (Accession NM_014833). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. KIAA1467 (Accession XM_049605) is another VGAM1077 host target gene. KIAA1467 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1467 BINDING SITE, designated SEQ ID:35456, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39304] Another function of VGAM1077 is therefore inhibition of KIAA1467 (Accession XM_049605). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1467. MO25 (Accession NM_016289) is another VGAM1077 host target gene. MO25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by MO25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MO25 BINDING SITE, designated SEQ ID:18416, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39305] Another function of VGAM1077 is therefore inhibition of MO25 (Accession NM_016289). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MO25. LOC129011 (Accession XM_059326) is another VGAM1077 host target gene. LOC129011 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129011 BINDING SITE, designated SEQ ID:36963, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39306] Another function of VGAM1077 is therefore inhibition of LOC129011 (Accession XM_059326). Accordingly, utilities

of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129011. LOC145945 (Accession XM_096908) is another VGAM1077 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40639, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39307] Another function of VGAM1077 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC148534 (Accession XM_086222) is another VGAM1077 host target gene. LOC148534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC148534 BINDING SITE, designated SEQ ID:38549, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39308] Another function of VGAM1077 is therefore inhibition of LOC148534 (Accession XM_086222). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148534. LOC150407 (Accession XM_086906) is another VGAM1077 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38949, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39309] Another function of VGAM1077 is therefore inhibition of LOC150407 (Accession XM_086906). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC221354 (Accession XM_166468) is another VGAM1077 host target gene. LOC221354 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221354 BINDING SITE, designated SEQ ID:44392, to the nucleotide sequence of VGAM1077 RNA, herein designated VGAM RNA, also designated SEQ ID:3788.

[39310] Another function of VGAM1077 is therefore inhibition of LOC221354 (Accession XM_166468). Accordingly, utilities of VGAM1077 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221354. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1078 (VGAM1078) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39311] VGAM1078 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1078 was detected is described hereinabove with reference to Figs. 1-8.

[39312] VGAM1078 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39313] VGAM1078 gene encodes a VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1078 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1078 precursor RNA is designated SEQ ID:1064, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1064 is located at position 1314 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39314] VGAM1078 precursor RNA folds onto itself, forming VGAM1078 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[39315] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1078 folded precursor RNA into VGAM1078 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1078 RNA is designated SEQ ID:3789, and is provided hereinbelow with reference to the sequence listing part.

[39316] VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1078 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39317] VGAM1078 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1078 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1078 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1078 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39318] The complementary binding of VGAM1078 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1078 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1078 host target RNA into VGAM1078 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39319] It is appreciated that VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1078 host target genes. The mRNA of each one of this plurality of VGAM1078 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1078 RNA, herein designated VGAM RNA, and which when bound by VGAM1078 RNA causes inhibition of translation of respective one or more VGAM1078 host target proteins.

[39320] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1078 gene, herein designated VGAM GENE, on one or more VGAM1078 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39321] It is yet further appreciated that a function of VGAM1078 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1078 correlate with, and may be deduced from, the identity of the host target genes which VGAM1078 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39322] Nucleotide sequences of the VGAM1078 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1078 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1078 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1078 are further described hereinbelow with reference to Table 1.

[39323] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1078 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1078 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39324] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1078 gene, herein designated VGAM is inhibition of expression of VGAM1078 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1078 correlate with, and may be deduced from, the identity of the target genes which VGAM1078 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39325] Active BCR-related Gene (ABR, Accession NM_001092) is a VGAM1078 host target gene. ABR BINDING SITE1 and ABR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of ABR BINDING SITE1 and ABR BINDING SITE2, designated SEQ ID:6748 and SEQ ID:22493 respectively, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39326] A function of VGAM1078 is therefore inhibition of Active BCR-related Gene (ABR, Accession NM_001092), a gene which gtpase-activating protein for rac and cdc42. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABR. The function of ABR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM489.Ephrin-A1 (EFNA1, Accession NM_004428) is another VGAM1078 host target gene. EFNA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNA1 BINDING SITE, designated SEQ ID:10703, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ

ID:3789.

[39327] Another function of VGAM1078 is therefore inhibition of Ephrin-A1 (EFNA1, Accession NM_004428), a gene which is a ligand of Eph-related receptor tyrosine kinases. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNA1. The function of EFNA1 has been established by previous studies. Holzman et al. (1990) characterized the product of B61, one of 3 novel genes whose expression in human umbilical vein endothelial cells is induced by tumor necrosis factor-alpha in the presence of cycloheximide (see OMIM Ref. No. 191163). Southern analysis suggested to them that it is an evolutionarily conserved single-copy gene. Although primarily a hydrophilic molecule, it contained both a hydrophobic N-terminal and a hydrophobic C-terminal region. The N-terminal region was typical of a signal peptide, which is consistent with the secreted nature of the protein. The mature form of the predicted protein consists of 187 amino acid residues with a predicted molecular weight of 22,000. Sequence analysis of cDNA clones showed that the protein product of B61 had no significant homology to previously described proteins. Later it was shown to be a

member of the subfamily of ligands that bind to the EPH group of receptor tyrosine kinases. These so-called LERK proteins, also called ephrins, share sequence similarity and are attached to the cell membrane by glycosylphosphatidylinositol (GPI) linkages or by a single transmembrane domain (Cerretti et al., 1996). See 179610 for additional information on ephrins and the Eph receptor family. Pandey et al. (1995) presented evidence that LERK1 is involved in TNF-alpha (OMIM Ref. No. 191160)-induced angiogenesis.

[39328] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39329] Cerretti, D. P.; Lyman, S. D.; Kozlosky, C. J.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Valentine, V.; Kirstein, M. N.; Shapiro, D. N.; Morris, S. W. : The genes encoding the Eph-related receptor tyrosine kinase ligands LERK-1 (EPLG1, Epl1), LERK-3 (EPLG3, Epl3), and LERK-4 (EPLG4, Epl4) are clustered on human chromosome 1 and mouse chromosome 3. *Genomics* 33: 277-282, 1996. ; and

[39330] Pandey, A.; Lindberg, R. A.; Dixit, V. M. : Receptor orphans find a family. *Curr. Biol.* 5: 986-989, 1995.

[39331] Further studies establishing the function and utilities of

EFNA1 are found in John Hopkins OMIM database record ID 191164, and in cited publications numbered 9824–9826 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Oxidised Low Density Lipoprotein (lectin-like) Receptor 1 (OLR1, Accession NM_002543) is another VGAM1078 host target gene. OLR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OLR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLR1 BINDING SITE, designated SEQ ID:8395, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39332] Another function of VGAM1078 is therefore inhibition of Oxidised Low Density Lipoprotein (lectin-like) Receptor 1 (OLR1, Accession NM_002543), a gene which is involved in degradation of oxidized LDL by vascular endothelial cells. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLR1. The function of OLR1 has been established by previous studies. Endothelial cell dysfunction or activation elicited by oxidatively modified low

density lipoprotein (OMIM Ref. No. Ox-LDL) has been implicated in the pathogenesis of atherosclerosis. Vascular endothelial cells internalize and degrade Ox-LDL through a putative receptor-mediated pathway that does not involve macrophage scavenger receptors (see OMIM Ref. No. MSR1; 153622). To identify genes encoding Ox-LDL receptors, Sawamura et al. (1997) transfected mammalian cells with a cDNA expression library derived from bovine aortic endothelial cells and assayed for uptake of labeled Ox-LDL. They recovered a cDNA encoding an Ox-LDL receptor, which they designated lectin-like Ox-LDL receptor-1 (LOX1). Immunofluorescence studies showed that bovine LOX1 is expressed on the cell surface. Sawamura et al. (1997) cloned a cDNA encoding the human homolog of LOX1 by screening a human lung cDNA library with the bovine LOX1 cDNA. Cells stably expressing human LOX1 showed uptake of labeled Ox-LDL. The predicted 273-amino acid human LOX1 protein is 72% identical to bovine LOX1. Its structure is similar to that of C-type lectins such as CD94 (KLRD1) and NKR-P1 (KLRB1). Northern blot analysis revealed that human LOX1 is expressed as a 2.8-kb mRNA in various tissues, with the most abundant expression in placenta. Yamanaka et al. (1998) de-

terminated that LOX1 is expressed in vascular-rich organs but not in lymphocytes. Yamanaka et al. (1998) found that the LOX1 gene spans approximately 15 kb and consists of 6 exons. By fluorescence in situ hybridization, they mapped the gene to 12p12–p13, where genes of the natural killer cell receptors are clustered.

[39333] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39334] Sawamura, T.; Kume, N.; Aoyama, T.; Moriwaki, H.; Hoshikawa, H.; Aiba, Y.; Tanaka, T.; Miwa, S.; Katsura, Y.; Kita, T.; Masaki, T. : An endothelial receptor for oxidized low-density lipoprotein. *Nature* 386: 73–77, 1997. ; and

[39335] Yamanaka, S.; Zhang, X.-Y.; Miura, K.; Kim, S.; Iwao, H. : The human gene encoding the lectin-type oxidized LDL receptor (OLR1) is a novel member of the natural killer gene complex with.

[39336] Further studies establishing the function and utilities of OLR1 are found in John Hopkins OMIM database record ID 602601, and in cited publications numbered 1112–1113 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Oncostatin M (OSM, Accession NM_020530) is another VGAM1078 host target

gene. OSM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSM BINDING SITE, designated SEQ ID:21753, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39337] Another function of VGAM1078 is therefore inhibition of Oncostatin M (OSM, Accession NM_020530), a gene which inhibits the proliferation of a number of tumor cell lines, caused an acute inflammatory reaction. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSM. The function of OSM has been established by previous studies. Oncostatin M, a glycoprotein with an approximate molecular weight of 28,000, was originally isolated from a conditioned medium of human leukemia cells that had been induced to differentiate into macrophage-like cells by treatment with phorbol 12-myristate 13-acetate (Zarling et al., 1986). OSM has the ability to inhibit the growth of human A375 melanoma cells but not normal human fibroblasts; hence, its name. Treatment

with recombinant OSM leads to the inhibition of proliferation and changes in cellular morphology of a number of tumor cell lines derived from a wide variety of tissue types. Rose and Bruce (1991) detected significant similarities in the primary amino acid sequences and predicted secondary structures of OSM, leukemia-inhibitory factor (LIF; 159540), granulocyte colony-stimulating factor (CSF3; 138970), and interleukin-6 (IL6; 147620). Using a panel of DNAs from interspecies somatic cell hybrids, they showed, furthermore, that OSM, like LIF, is located on human chromosome 22. They also demonstrated that OSM has the ability to inhibit the proliferation of murine M1 myeloid leukemic cells and can induce their differentiation into macrophage-like cells, a function shared by LIF, CSF3, and IL6. They proposed that these 4 molecules are structurally related members of a cytokine family that have in common the ability to modulate differentiation of a variety of cell types. Although oncostatin M inhibits the growth of a variety of cancer and other cells, Nair et al. (1992) and Miles et al. (1992) found that it is a potent mitogen for cells derived from HIV-related Kaposi sarcoma (OMIM Ref. No. 148000). Rose et al. (1993) found that the genes for OSM and LIF were segregating when cDNA

probes were hybridized to DNA from somatic cell hybrids containing defined regions of human chromosome 22. They found a contig of approximately 100 kb surrounding the 2 genes which were tandemly arranged in the same transcriptional orientation and separated by approximately 10 kb. The direction of gene transcription was telomeric to centromeric, with the OSM gene located upstream of the LIF gene. The findings constituted strong evidence that OSM and LIF resulted from duplication of a common ancestral gene. Oncostatin M is a member of the IL-6 family of cytokines that is primarily known for its effects on cell growth. In exploration of the potential of oncostatin M as an inflammatory effector, Modur et al. (1997) found that oncostatin M caused an acute inflammatory reaction in vivo and that it colocalized with TNF-secreting cells in chronically inflamed human vascular tissue. It induced transmigration of human neutrophils through monolayers of endothelial cells by stimulating the expression of adhesion molecules and chemokines. The pattern of endothelial cell responses, however, significantly differed from the response to TNF (OMIM Ref. No. 191160). Modur et al. (1997) concluded that oncostatin M, but not other IL-6 family members, fulfilled Koch's postu-

lates as an inflammatory mediator. Since its effects on endothelial cells differ significantly from established mediators like TNF- α , it may uniquely contribute to the inflammatory cycle.

[39338] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39339] Rose, T. M.; Bruce, A. G. : Oncostatin M is a member of a cytokine family that includes leukemia-inhibitory factor, granulocyte colony-stimulating factor, and interleukin 6. Proc. Nat. Acad. Sci. 88: 8641-8645, 1991. ; and

[39340] Modur, V.; Feldhaus, M. J.; Weyrich, A. S.; Jicha, D. L.; Prescott, S. M.; Zimmerman, G. A.; McIntyre, T. M. : Oncostatin M is a proinflammatory mediator: in vivo effects correlate with end.

[39341] Further studies establishing the function and utilities of OSM are found in John Hopkins OMIM database record ID 165095, and in cited publications numbered 2970-297 and 11683 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Paired Box Gene 2 (PAX2, Accession NM_003987) is another VGAM1078 host target gene. PAX2 BINDING SITE1 and PAX2 BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by PAX2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAX2 BINDING SITE1 and PAX2 BINDING SITE2, designated SEQ ID:10136 and SEQ ID:10142 respectively, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39342] Another function of VGAM1078 is therefore inhibition of Paired Box Gene 2 (PAX2, Accession NM_003987), a gene which involves in kidney cell differentiation. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX2. The function of PAX2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM407.S100 Calcium Binding Protein, Beta (neural) (S100B, Accession NM_006272) is another VGAM1078 host target gene. S100B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by S100B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of S100B BINDING SITE, designated SEQ ID:12955, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39343] Another function of VGAM1078 is therefore inhibition of S100 Calcium Binding Protein, Beta (neural) (S100B, Accession NM_006272), a gene which weakly binds calcium but binds zinc very tightly—distinct binding sites with different affinities exist for both ions on each monomer. Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with S100B. The function of S100B has been established by previous studies. See 176940. The beta-subunit of S100 protein is expressed in glial cells at levels at least tenfold higher than in most other cell types. The brain also contains small amounts of the alpha subunits at levels approximately one-tenth that of the beta subunit. Allore et al. (1988) used genomic and cDNA probes in connection with a panel of rodent-human somatic cell hybrids to assign the S100B gene to 21q22. They suggested that this is a candidate gene for the neurologic disturbances in Down syndrome when present in trisomic state. By in situ hybridization, Duncan et al. (1989) localized the

S100B gene to 21q22.2–q22.3. Allore et al. (1990) isolated overlapping genomic clones spanning the region coding for S100B and its flanking sequences. The intron/exon organization is similar to that of the genes coding for several other members of the S100 protein subfamily. The S100B gene is composed of 3 exons, the first of which specifies the 5–prime untranslated region. Morii et al. (1991) isolated the S100A (OMIM Ref. No. 176940) and S100B genes from a human genomic DNA library. Endonuclease mapping and DNA sequencing showed that both comprise 3 exons and 2 introns. Two $\text{Ca}(2+)$ –binding domains were independently encoded by exons 2 and 3. By spot–blot hybridization analysis of flow–sorted chromosomes, Morii et al. (1991) showed that the S100A and S100B genes are located on chromosome 1 and chromosome 21, respectively. Using restriction endonuclease fragment length variations (RFLV) in multipoint backcrosses, Shimizu et al. (1992) mapped the S100b gene in relation to other genes on mouse chromosome 10. The S100B gene is expressed at high levels in brain primarily by astrocytes. Addition of the disulfide–bonded dimeric form of the protein to primary neuronal and glial cultures and established cell lines induces axonal

extension and alterations in astrocyte proliferation and phenotype. Reeves et al. (1994) demonstrated that the same effects of the S100B protein are exerted in vivo. They found that both astrocytosis and neurite proliferation occurred in transgenic mice expressing elevated levels of S100b. They suggested that these transgenic mice represent a useful model for studies of the role of S100B in glial-neuronal interactions in normal development and function of the brain and for analyzing the significance of elevated levels of the protein in Down syndrome and Alzheimer disease.

[39344] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39345] Reeves, R. H.; Yao, J.; Crowley, M. R.; Buck, S.; Zhang, X.; Yarowsky, P.; Gearhart, J. D.; Hilt, D. C. : Astrocytosis and axonal proliferation in the hippocampus of S100b transgenic mice. *Proc. Nat. Acad. Sci.* 91: 5359–5363, 1994. ; and

[39346] Shimizu, A.; Sakai, Y.; Ohno, K.; Masaki, S.; Kuwano, R.; Takahashi, Y.; Miyashita, N.; Watanabe, T. : A molecular genetic linkage map of mouse chromosome 10, including the Myb, S100b, P.

[39347] Further studies establishing the function and utilities of S100B are found in John Hopkins OMIM database record ID 176990, and in cited publications numbered 888–890, 1236 and 2742 listed in the bibliography section herein–below, which are also hereby incorporated by reference. SH3–domain Binding Protein 2 (SH3BP2, Accession NM_003023) is another VGAM1078 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2 BINDING SITE, designated SEQ ID:8946, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39348] Another function of VGAM1078 is therefore inhibition of SH3–domain Binding Protein 2 (SH3BP2, Accession NM_003023). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP2. DKFZP566K023 (Accession NM_015485) is another VGAM1078 host target gene. DKFZP566K023 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by DKFZP566K023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566K023 BINDING SITE, designated SEQ ID:17759, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39349] Another function of VGAM1078 is therefore inhibition of DKFZP566K023 (Accession NM_015485). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566K023. ELKS (Accession NM_015064) is another VGAM1078 host target gene. ELKS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELKS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELKS BINDING SITE, designated SEQ ID:17419, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39350] Another function of VGAM1078 is therefore inhibition of

ELKS (Accession NM_015064). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELKS. FLJ20371 (Accession NM_017791) is another VGAM1078 host target gene. FLJ20371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20371 BINDING SITE, designated SEQ ID:19424, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39351] Another function of VGAM1078 is therefore inhibition of FLJ20371 (Accession NM_017791). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20371. FLJ23071 (Accession NM_025192) is another VGAM1078 host target gene. FLJ23071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ23071 BINDING SITE, designated SEQ ID:24846, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39352] Another function of VGAM1078 is therefore inhibition of FLJ23071 (Accession NM_025192). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23071. Hydroxysteroid (17-beta) Dehydrogenase 12 (HSD17B12, Accession NM_016142) is another VGAM1078 host target gene. HSD17B12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSD17B12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSD17B12 BINDING SITE, designated SEQ ID:18225, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39353] Another function of VGAM1078 is therefore inhibition of Hydroxysteroid (17-beta) Dehydrogenase 12 (HSD17B12, Accession NM_016142). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with HSD17B12. HT002 (Accession NM_014066) is another VGAM1078 host target gene. HT002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HT002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HT002 BINDING SITE, designated SEQ ID:15282, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39354] Another function of VGAM1078 is therefore inhibition of HT002 (Accession NM_014066). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HT002. KIAA0061 (Accession XM_043094) is another VGAM1078 host target gene. KIAA0061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0061 BINDING SITE, designated SEQ ID:33891, to the nucleotide sequence of

VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39355] Another function of VGAM1078 is therefore inhibition of KIAA0061 (Accession XM_043094). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0061. KIAA0252 (Accession XM_031646) is another VGAM1078 host target gene. KIAA0252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0252 BINDING SITE, designated SEQ ID:31447, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39356] Another function of VGAM1078 is therefore inhibition of KIAA0252 (Accession XM_031646). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0252. KIAA0729 (Accession XM_171027) is another VGAM1078 host target gene. KIAA0729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0729 BINDING SITE, designated SEQ ID:45804, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39357] Another function of VGAM1078 is therefore inhibition of KIAA0729 (Accession XM_171027). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0729. Lipase, Endothelial (LIPG, Accession NM_006033) is another VGAM1078 host target gene. LIPG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIPG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPG BINDING SITE, designated SEQ ID:12653, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39358] Another function of VGAM1078 is therefore inhibition of Lipase, Endothelial (LIPG, Accession NM_006033). Accord-

ingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPG. Synaptopodin 2 (SYNPO2, Accession XM_050219) is another VGAM1078 host target gene. SYNPO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNPO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNPO2 BINDING SITE, designated SEQ ID:35592, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39359] Another function of VGAM1078 is therefore inhibition of Synaptopodin 2 (SYNPO2, Accession XM_050219). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNPO2. TBLR1 (Accession NM_024665) is another VGAM1078 host target gene. TBLR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBLR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TBLR1 BINDING SITE, designated SEQ ID:23964, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39360] Another function of VGAM1078 is therefore inhibition of TBLR1 (Accession NM_024665). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBLR1. Zinc Finger Protein 300 (ZNF300, Accession NM_052860) is another VGAM1078 host target gene. ZNF300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF300 BINDING SITE, designated SEQ ID:27439, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39361] Another function of VGAM1078 is therefore inhibition of Zinc Finger Protein 300 (ZNF300, Accession NM_052860). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF300. LOC145757 (Accession

XM_085227) is another VGAM1078 host target gene.

LOC145757 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145757, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145757 BINDING SITE, designated SEQ ID:37968, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39362] Another function of VGAM1078 is therefore inhibition of LOC145757 (Accession XM_085227). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145757. LOC145945 (Accession XM_096908) is another VGAM1078 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40629, to the nucleotide sequence of VGAM1078 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3789.

[39363] Another function of VGAM1078 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC152190 (Accession XM_045692) is another VGAM1078 host target gene. LOC152190 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152190 BINDING SITE, designated SEQ ID:34524, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39364] Another function of VGAM1078 is therefore inhibition of LOC152190 (Accession XM_045692). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152190. LOC201164 (Accession XM_113904) is another VGAM1078 host target gene. LOC201164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201164, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201164 BINDING SITE, designated SEQ ID:42528, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39365] Another function of VGAM1078 is therefore inhibition of LOC201164 (Accession XM_113904). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201164. LOC219899 (Accession XM_166173) is another VGAM1078 host target gene. LOC219899 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219899 BINDING SITE, designated SEQ ID:43988, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39366] Another function of VGAM1078 is therefore inhibition of LOC219899 (Accession XM_166173). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC219899. LOC220883 (Accession XM_166076) is another VGAM1078 host target gene. LOC220883 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220883 BINDING SITE, designated SEQ ID:43848, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39367] Another function of VGAM1078 is therefore inhibition of LOC220883 (Accession XM_166076). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220883. LOC255520 (Accession XM_171073) is another VGAM1078 host target gene. LOC255520 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255520 BINDING SITE, designated SEQ ID:45877, to

the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39368] Another function of VGAM1078 is therefore inhibition of LOC255520 (Accession XM_171073). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255520. LOC255919 (Accession XM_170794) is another VGAM1078 host target gene. LOC255919 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255919 BINDING SITE, designated SEQ ID:45556, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39369] Another function of VGAM1078 is therefore inhibition of LOC255919 (Accession XM_170794). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255919. LOC257355 (Accession XM_170482) is another VGAM1078 host target gene. LOC257355 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257355 BINDING SITE, designated SEQ ID:45321, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39370] Another function of VGAM1078 is therefore inhibition of LOC257355 (Accession XM_170482). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257355. LOC51172 (Accession XM_032690) is another VGAM1078 host target gene. LOC51172 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51172 BINDING SITE, designated SEQ ID:31720, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39371] Another function of VGAM1078 is therefore inhibition of LOC51172 (Accession XM_032690). Accordingly, utilities

of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51172. LOC89231 (Accession XM_166577) is another VGAM1078 host target gene. LOC89231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89231 BINDING SITE, designated SEQ ID:44550, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39372] Another function of VGAM1078 is therefore inhibition of LOC89231 (Accession XM_166577). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89231. LOC90639 (Accession XM_033092) is another VGAM1078 host target gene. LOC90639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90639 BINDING SITE, designated SEQ ID:31832, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39373] Another function of VGAM1078 is therefore inhibition of LOC90639 (Accession XM_033092). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90639. LOC91565 (Accession XM_039231) is another VGAM1078 host target gene. LOC91565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91565 BINDING SITE, designated SEQ ID:33022, to the nucleotide sequence of VGAM1078 RNA, herein designated VGAM RNA, also designated SEQ ID:3789.

[39374] Another function of VGAM1078 is therefore inhibition of LOC91565 (Accession XM_039231). Accordingly, utilities of VGAM1078 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91565. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1079 (VGAM1079) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39375] VGAM1079 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1079 was detected is described hereinabove with reference to Figs. 1–8.

[39376] VGAM1079 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39377] VGAM1079 gene encodes a VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1079 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1079 precursor RNA is designated SEQ ID:1065, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1065 is located at position 5967 relative to the

genome of Porcine Epidemic Diarrhea Virus.

[39378] VGAM1079 precursor RNA folds onto itself, forming VGAM1079 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39379] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1079 folded precursor RNA into VGAM1079 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1079 RNA is designated SEQ ID:3790, and is provided hereinbelow with reference to the sequence listing part.

[39380] VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1079 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39381] VGAM1079 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1079 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1079 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39382] The complementary binding of VGAM1079 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1079 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1079 host target RNA into VGAM1079 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39383] It is appreciated that VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1079 host target genes. The mRNA of each one of this plurality of VGAM1079 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1079 RNA, herein designated VGAM RNA, and which when bound by VGAM1079 RNA causes inhibition of translation of respective one or more VGAM1079 host target proteins.

[39384] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1079 gene, herein designated VGAM GENE, on one or more VGAM1079 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39385] It is yet further appreciated that a function of VGAM1079 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of

VGAM1079 correlate with, and may be deduced from, the identity of the host target genes which VGAM1079 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39386] Nucleotide sequences of the VGAM1079 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1079 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1079 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1079 are further described hereinbelow with reference to Table 1.

[39387] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1079 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1079 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39388] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1079 gene, herein designated VGAM is inhibition of expression of VGAM1079 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1079 correlate with, and may be deduced

from, the identity of the target genes which VGAM1079 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39389] CGTHBA (Accession NM_012075) is a VGAM1079 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14363, to the nucleotide sequence of VGAM1079 RNA, herein designated VGAM RNA, also designated SEQ ID:3790.

[39390] A function of VGAM1079 is therefore inhibition of CGTHBA (Accession NM_012075). Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Chloride Channel 6 (CLCN6, Accession NM_021735) is another VGAM1079 host target gene. CLCN6 BINDING SITE1 through CLCN6 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CLCN6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING

SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN6 BINDING SITE1 through CLCN6 BINDING SITE3, designated SEQ ID:22336, SEQ ID:6959 and SEQ ID:22341 respectively, to the nucleotide sequence of VGAM1079 RNA, herein designated VGAM RNA, also designated SEQ ID:3790.

[39391] Another function of VGAM1079 is therefore inhibition of Chloride Channel 6 (CLCN6, Accession NM_021735), a gene which is a voltage-gated chloride channel. Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN6. The function of CLCN6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM599.LBP-9 (Accession NM_014553) is another VGAM1079 host target gene. LBP-9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBP-9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBP-9 BINDING SITE, designated SEQ ID:15873, to the nucleotide sequence of VGAM1079 RNA, herein designated

VGAM RNA, also designated SEQ ID:3790.

[39392] Another function of VGAM1079 is therefore inhibition of LBP-9 (Accession NM_014553). Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LBP-9. Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255) is another VGAM1079 host target gene. MRPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL10 BINDING SITE, designated SEQ ID:29767, to the nucleotide sequence of VGAM1079 RNA, herein designated VGAM RNA, also designated SEQ ID:3790.

[39393] Another function of VGAM1079 is therefore inhibition of Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255). Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL10. LOC202126 (Accession XM_117362) is another VGAM1079 host target gene. LOC202126 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by LOC202126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202126 BINDING SITE, designated SEQ ID:43411, to the nucleotide sequence of VGAM1079 RNA, herein designated VGAM RNA, also designated SEQ ID:3790.

[39394] Another function of VGAM1079 is therefore inhibition of LOC202126 (Accession XM_117362). Accordingly, utilities of VGAM1079 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202126. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1080 (VGAM1080) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39395] VGAM1080 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1080 was detected is described hereinabove with reference to Figs. 1-8.

[39396] VGAM1080 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39397] VGAM1080 gene encodes a VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1080 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1080 precursor RNA is designated SEQ ID:1066, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1066 is located at position 15169 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39398] VGAM1080 precursor RNA folds onto itself, forming VGAM1080 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[39399] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1080 folded precursor RNA into VGAM1080 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1080 RNA is designated SEQ ID:3791, and is provided hereinbelow with reference to the sequence listing part.

[39400] VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1080 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39401] VGAM1080 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1080 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1080 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1080 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39402] The complementary binding of VGAM1080 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1080 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1080 host target RNA into VGAM1080 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39403] It is appreciated that VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1080 host target genes. The mRNA of each one of this plurality of VGAM1080 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1080 RNA, herein designated VGAM RNA, and which when bound by VGAM1080 RNA causes inhibition of translation of respective one or more VGAM1080 host target proteins.

[39404] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1080 gene, herein designated VGAM GENE, on one or more VGAM1080 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39405] It is yet further appreciated that a function of VGAM1080 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1080 correlate with, and may be deduced from, the identity of the host target genes which VGAM1080 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39406] Nucleotide sequences of the VGAM1080 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1080 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1080 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1080 are further described hereinbelow with reference to Table 1.

[39407] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1080 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1080 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39408] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1080 gene, herein designated VGAM is inhibition of expression of VGAM1080 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1080 correlate with, and may be deduced from, the identity of the target genes which VGAM1080 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39409] UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1) (GALNT1, Accession NM_020474) is a VGAM1080 host target gene. GALNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT1 BINDING SITE, designated SEQ ID:21726, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39410] A function of VGAM1080 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1) (GALNT1, Accession NM_020474), a gene which transfers an N-acetyl galactosamine (GalNAc) to a serine or threonine residue in the first step of O-linked oligosaccharide biosynthesis. Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT1. The function of GALNT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Cytoskeleton-associated Protein 4 (CKAP4, Accession NM_006825) is another VGAM1080 host target gene. CKAP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKAP4, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKAP4 BINDING SITE, designated SEQ ID:13706, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39411] Another function of VGAM1080 is therefore inhibition of Cytoskeleton-associated Protein 4 (CKAP4, Accession NM_006825). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKAP4. FLJ13081 (Accession NM_024834) is another VGAM1080 host target gene. FLJ13081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13081 BINDING SITE, designated SEQ ID:24238, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39412] Another function of VGAM1080 is therefore inhibition of FLJ13081 (Accession NM_024834). Accordingly, utilities of

VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13081. FLJ23024 (Accession NM_024936) is another VGAM1080 host target gene. FLJ23024 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23024 BINDING SITE, designated SEQ ID:24475, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39413] Another function of VGAM1080 is therefore inhibition of FLJ23024 (Accession NM_024936). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23024. KIAA0121 (Accession XM_052386) is another VGAM1080 host target gene. KIAA0121 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0121 BINDING SITE, designated SEQ ID:35971, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39414] Another function of VGAM1080 is therefore inhibition of KIAA0121 (Accession XM_052386). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379) is another VGAM1080 host target gene. SEMA3C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3C BINDING SITE, designated SEQ ID:13076, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39415] Another function of VGAM1080 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379). Accordingly, utilities of VGAM1080 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3C. Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832) is another VGAM1080 host target gene. SLC26A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC26A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A7 BINDING SITE, designated SEQ ID:27415, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39416] Another function of VGAM1080 is therefore inhibition of Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A7. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863) is another VGAM1080 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11284, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39417] Another function of VGAM1080 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. LOC145748 (Accession XM_096853) is another VGAM1080 host target gene. LOC145748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145748 BINDING SITE, designated SEQ ID:40580, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39418] Another function of VGAM1080 is therefore inhibition of LOC145748 (Accession XM_096853). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145748. LOC91145 (Accession XM_036454) is another VGAM1080 host target gene. LOC91145 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91145 BINDING SITE, designated SEQ ID:32450, to the nucleotide sequence of VGAM1080 RNA, herein designated VGAM RNA, also designated SEQ ID:3791.

[39419] Another function of VGAM1080 is therefore inhibition of LOC91145 (Accession XM_036454). Accordingly, utilities of VGAM1080 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91145. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1081 (VGAM1081) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39420] VGAM1081 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1081 was detected is described hereinabove with reference to Figs. 1–8.

[39421] VGAM1081 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39422] VGAM1081 gene encodes a VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1081 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1081 precursor RNA is designated SEQ ID:1067, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1067 is located at position 11817 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39423] VGAM1081 precursor RNA folds onto itself, forming VGAM1081 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39424] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1081 folded precursor RNA into VGAM1081 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1081 RNA is designated SEQ ID:3792, and is provided hereinbelow with reference to the sequence listing part.

[39425] VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1081 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39426] VGAM1081 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1081 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1081 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39427] The complementary binding of VGAM1081 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1081 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1081 host target RNA into VGAM1081 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39428] It is appreciated that VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1081 host target genes. The mRNA of each one of this plurality of VGAM1081 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1081 RNA, herein designated VGAM RNA, and which when bound by VGAM1081 RNA causes inhibition of translation of respective one or more VGAM1081 host target proteins.

[39429] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1081 gene, herein designated VGAM GENE, on one or more VGAM1081 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39430] It is yet further appreciated that a function of VGAM1081 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1081 correlate with, and may be deduced from, the identity of the host target genes which VGAM1081 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39431] Nucleotide sequences of the VGAM1081 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1081 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1081 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1081 are further described hereinbelow with reference to Table 1.

[39432] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1081 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1081 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39433] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1081 gene, herein designated VGAM is inhibition of expression of VGAM1081 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1081 correlate with, and may be deduced from, the identity of the target genes which VGAM1081 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39434] Calpain 10 (CAPN10, Accession NM_023088) is a VGAM1081 host target gene. CAPN10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by CAPN10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN10 BINDING SITE, designated SEQ ID:23356, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39435] A function of VGAM1081 is therefore inhibition of Calpain 10 (CAPN10, Accession NM_023088), a gene which catalyzes limited proteolysis of substrates involved in cytoskeletal remodelling and signal transduction. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN10. The function of CAPN10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Endoglin (Osler-Rendu-Weber syndrome 1) (ENG, Accession NM_000118) is another VGAM1081 host target gene. ENG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of ENG BINDING SITE, designated SEQ ID:5591, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39436] Another function of VGAM1081 is therefore inhibition of Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM_000118). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENG. LARS2 (Accession NM_015340) is another VGAM1081 host target gene. LARS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LARS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LARS2 BINDING SITE, designated SEQ ID:17648, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39437] Another function of VGAM1081 is therefore inhibition of LARS2 (Accession NM_015340). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LARS2.

Membrane Component, Chromosome 17, Surface Marker 2 (ovarian carcinoma antigen CA125) (M17S2, Accession NM_031858) is another VGAM1081 host target gene. M17S2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by M17S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M17S2 BINDING SITE, designated SEQ ID:25610, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39438] Another function of VGAM1081 is therefore inhibition of Membrane Component, Chromosome 17, Surface Marker 2 (ovarian carcinoma antigen CA125) (M17S2, Accession NM_031858), a gene which Contains a B-box/coiled coil motif. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M17S2. The function of M17S2 has been established by previous studies. In an attempt to clone the CA125 gene (OMIM Ref. No. 606154), Campbell et al. (1994) isolated a cDNA from an expression library that mapped close to the BRCA1 locus (OMIM Ref. No.

113705) at 17q21.1. Closer investigation showed that it was within the smallest known region containing the BRCA1 gene. The predicted 966–amino acid polypeptide lacks the membrane protein characteristics expected for CA125 but does include a B–box/coiled coil motif present in many genes with transformation potential. Campbell et al. (1994) used fluorescence in situ hybridization to demonstrate mapping within the BRCA1 minimum region. YAC and cosmid clones were isolated and used to refine the location of this gene adjacent and proximal to the RNU2 locus (OMIM Ref. No. 180690). The exon structure of the gene was also determined. Extensive SSCP and sequence analysis of over 100 tumor and normal DNAs from familial and sporadic breast cancers and sporadic ovarian cancers failed to detect mutations in the coding region of this gene. Brown et al. (1994), who referred to the gene as 1A1–3B, showed that the transcription start site of M17S2 is 295 bp distal from the initiation site of BRCA1 and that the gene is transcribed divergently from BRCA1. The authors speculated that M17S2 may be involved in the regulation of transcription or translation of BRCA1. Brown et al. (1996) described the genomic region that encompasses both the BRCA1 and M17S2 genes. They found a tandem

duplication of 30 kb that results in 2 copies of exons 1 and 2 of BRCA1 and exons 1 and 3 of M17S2.

[39439] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39440] Brown, M. A.; Xu, C.-F.; Nicolai, H.; Griffiths, B.; Chambers, J. A.; Black, D.; Solomon, E. : The 5-prime end of the BRCA1 gene lies within a duplicated region of human chromosome 17q21. *Oncogene* 12: 2507-2513, 1996. ; and

[39441] Campbell, I. G.; Nicolai, H. M.; Foulkes, W. D.; Senger, G.; Stamp, G. W.; Allan, G.; Boyer, C.; Jones, K.; Bast, R. C., Jr.; Solomon, E.; Trowsdale, J.; Black, D. M. : A novel gene encoding.

[39442] Further studies establishing the function and utilities of M17S2 are found in John Hopkins OMIM database record ID 166945, and in cited publications numbered 1815-1817 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mannan-binding Lectin Serine Protease 1 (C4/C2 activating component of Ra-reactive factor) (MASP1, Accession NM_001879) is another VGAM1081 host target gene. MASP1 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by MASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MASP1 BINDING SITE, designated SEQ ID:7608, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39443] Another function of VGAM1081 is therefore inhibition of Mannan-binding Lectin Serine Protease 1 (C4/C2 activating component of Ra-reactive factor) (MASP1, Accession NM_001879), a gene which a complement-dependent bactericidal factor . Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MASP1. The function of MASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM566. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 2 (MLLT2, Accession NM_005935) is another VGAM1081 host target gene. MLLT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by MLLT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT2 BINDING SITE, designated SEQ ID:12574, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39444] Another function of VGAM1081 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 2 (MLLT2, Accession NM_005935), a gene which is a Putative transcription factor. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT2. The function of MLLT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. MAX Binding Protein (MNT, Accession NM_020310) is another VGAM1081 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21567, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39445] Another function of VGAM1081 is therefore inhibition of MAX Binding Protein (MNT, Accession NM_020310). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Mature T-cell Proliferation 1 (MTCP1, Accession NM_014221) is another VGAM1081 host target gene. MTCP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MTCP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTCP1 BINDING SITE, designated SEQ ID:15489, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39446] Another function of VGAM1081 is therefore inhibition of Mature T-cell Proliferation 1 (MTCP1, Accession NM_014221). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MTCP1. Nuclear Receptor Coactivator 6 (NCOA6, Accession NM_014071) is another VGAM1081 host target gene. NCOA6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NCOA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA6 BINDING SITE, designated SEQ ID:15288, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39447] Another function of VGAM1081 is therefore inhibition of Nuclear Receptor Coactivator 6 (NCOA6, Accession NM_014071), a gene which activates gene transcription through ligand-dependent association with coactivators. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA6. The function of NCOA6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM_006165) is another VGAM1081 host target gene.

NFRKB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NFRKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFRKB BINDING SITE, designated SEQ ID:12823, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39448] Another function of VGAM1081 is therefore inhibition of Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM_006165). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFRKB. Plexin A2 (PLXNA2, Accession NM_025179) is another VGAM1081 host target gene. PLXNA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PLXNA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLXNA2 BINDING SITE, designated SEQ ID:24816, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM

RNA, also designated SEQ ID:3792.

[39449] Another function of VGAM1081 is therefore inhibition of Plexin A2 (PLXNA2, Accession NM_025179), a gene which is a transmembrane protein. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLXNA2. The function of PLXNA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan) (SDC2, Accession XM_040582) is another VGAM1081 host target gene. SDC2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SDC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC2 BINDING SITE, designated SEQ ID:33327, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39450] Another function of VGAM1081 is therefore inhibition of Syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan) (SDC2, Accession XM_040582).

Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC2. Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM_000351) is another VGAM1081 host target gene. STS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STS BINDING SITE, designated SEQ ID:5908, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39451] Another function of VGAM1081 is therefore inhibition of Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM_000351). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STS. Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481) is another VGAM1081 host target gene. TCF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF2, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE, designated SEQ ID:13203, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39452] Another function of VGAM1081 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118.T-cell Leukemia Translocation Altered Gene (TCTA, Accession NM_022171) is another VGAM1081 host target gene. TCTA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCTA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TCTA BINDING SITE, designated SEQ ID:22732, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39453] Another function of VGAM1081 is therefore inhibition of T-cell Leukemia Translocation Altered Gene (TCTA, Accession NM_022171). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCTA. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728) is another VGAM1081 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38839, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39454] Another function of VGAM1081 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728). Accordingly, utilities of

VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. Chromosome 20 Open Reading Frame 42 (C20orf42, Accession NM_017671) is another VGAM1081 host target gene. C20orf42 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf42 BINDING SITE, designated SEQ ID:19216, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39455] Another function of VGAM1081 is therefore inhibition of Chromosome 20 Open Reading Frame 42 (C20orf42, Accession NM_017671). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf42. Diacylglycerol Kinase, Zeta 104kDa (DGKZ, Accession NM_003646) is another VGAM1081 host target gene. DGKZ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DGKZ, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKZ BINDING SITE, designated SEQ ID:9722, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39456] Another function of VGAM1081 is therefore inhibition of Diacylglycerol Kinase, Zeta 104kDa (DGKZ, Accession NM_003646). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKZ. FLJ10097 (Accession XM_043653) is another VGAM1081 host target gene. FLJ10097 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10097 BINDING SITE, designated SEQ ID:33989, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39457] Another function of VGAM1081 is therefore inhibition of FLJ10097 (Accession XM_043653). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10097. FLJ20686 (Accession NM_017925) is another VGAM1081 host target gene. FLJ20686 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20686 BINDING SITE, designated SEQ ID:19597, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39458] Another function of VGAM1081 is therefore inhibition of FLJ20686 (Accession NM_017925). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20686. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM1081 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE,

designated SEQ ID:7865, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39459] Another function of VGAM1081 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379) is another VGAM1081 host target gene. KCNV1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNV1 BINDING SITE, designated SEQ ID:15713, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39460] Another function of VGAM1081 is therefore inhibition of Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with KCNV1. LAT1-3TM (Accession NM_031211) is another VGAM1081 host target gene. LAT1-3TM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LAT1-3TM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAT1-3TM BINDING SITE, designated SEQ ID:25252, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39461] Another function of VGAM1081 is therefore inhibition of LAT1-3TM (Accession NM_031211). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAT1-3TM. MCF.2 Cell Line Derived Transforming Sequence-like (MCF2L, Accession XM_027516) is another VGAM1081 host target gene. MCF2L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MCF2L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCF2L BINDING SITE,

designated SEQ ID:30510, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39462] Another function of VGAM1081 is therefore inhibition of MCF.2 Cell Line Derived Transforming Sequence-like (MCF2L, Accession XM_027516). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCF2L. MGC5601 (Accession NM_025247) is another VGAM1081 host target gene. MGC5601 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5601, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5601 BINDING SITE, designated SEQ ID:24927, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39463] Another function of VGAM1081 is therefore inhibition of MGC5601 (Accession NM_025247). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5601. NBR2 (Accession NM_005821) is another

VGAM1081 host target gene. NBR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NBR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBR2 BINDING SITE, designated SEQ ID:12426, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39464] Another function of VGAM1081 is therefore inhibition of NBR2 (Accession NM_005821). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBR2. Phosphatidylethanolamine N-methyltransferase (PEMT, Accession NM_007169) is another VGAM1081 host target gene. PEMT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PEMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEMT BINDING SITE, designated SEQ ID:14014, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39465] Another function of VGAM1081 is therefore inhibition of Phosphatidylethanolamine N-methyltransferase (PEMT, Accession NM_007169). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEMT. Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B", Alpha (PPP2R3A, Accession NM_002718) is another VGAM1081 host target gene. PPP2R3A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP2R3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R3A BINDING SITE, designated SEQ ID:8586, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39466] Another function of VGAM1081 is therefore inhibition of Protein Phosphatase 2 (formerly 2A), Regulatory Subunit B", Alpha (PPP2R3A, Accession NM_002718). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R3A. LOC119188 (Accession XM_058373) is another VGAM1081 host target gene. LOC119188 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC119188, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119188 BINDING SITE, designated SEQ ID:36612, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39467] Another function of VGAM1081 is therefore inhibition of LOC119188 (Accession XM_058373). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119188. LOC143153 (Accession XM_084440) is another VGAM1081 host target gene. LOC143153 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143153 BINDING SITE, designated SEQ ID:37579, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39468] Another function of VGAM1081 is therefore inhibition of

LOC143153 (Accession XM_084440). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143153. LOC143154 (Accession XM_084441) is another VGAM1081 host target gene. LOC143154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143154 BINDING SITE, designated SEQ ID:37586, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39469] Another function of VGAM1081 is therefore inhibition of LOC143154 (Accession XM_084441). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143154. LOC148195 (Accession XM_097419) is another VGAM1081 host target gene. LOC148195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC148195 BINDING SITE, designated SEQ ID:40874, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39470] Another function of VGAM1081 is therefore inhibition of LOC148195 (Accession XM_097419). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148195. LOC149010 (Accession XM_086397) is another VGAM1081 host target gene. LOC149010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149010 BINDING SITE, designated SEQ ID:38630, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39471] Another function of VGAM1081 is therefore inhibition of LOC149010 (Accession XM_086397). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149010. LOC149182 (Accession XM_097605) is an-

other VGAM1081 host target gene. LOC149182 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149182 BINDING SITE, designated SEQ ID:40970, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39472] Another function of VGAM1081 is therefore inhibition of LOC149182 (Accession XM_097605). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149182. LOC150159 (Accession NM_139173) is another VGAM1081 host target gene. LOC150159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150159 BINDING SITE, designated SEQ ID:29180, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39473] Another function of VGAM1081 is therefore inhibition of LOC150159 (Accession NM_139173). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150159. LOC197423 (Accession XM_085436) is another VGAM1081 host target gene. LOC197423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197423 BINDING SITE, designated SEQ ID:38142, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39474] Another function of VGAM1081 is therefore inhibition of LOC197423 (Accession XM_085436). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197423. LOC200597 (Accession XM_114266) is another VGAM1081 host target gene. LOC200597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200597, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200597 BINDING SITE, designated SEQ ID:42826, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39475] Another function of VGAM1081 is therefore inhibition of LOC200597 (Accession XM_114266). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200597. LOC204970 (Accession XM_114795) is another VGAM1081 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43069, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39476] Another function of VGAM1081 is therefore inhibition of LOC204970 (Accession XM_114795). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC204970. LOC219294 (Accession XM_167566) is another VGAM1081 host target gene. LOC219294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219294 BINDING SITE, designated SEQ ID:44686, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39477] Another function of VGAM1081 is therefore inhibition of LOC219294 (Accession XM_167566). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219294. LOC219295 (Accession XM_167565) is another VGAM1081 host target gene. LOC219295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219295 BINDING SITE, designated SEQ ID:44681, to the nucleotide sequence of VGAM1081 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3792.

[39478] Another function of VGAM1081 is therefore inhibition of LOC219295 (Accession XM_167565). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219295. LOC219513 (Accession XM_169166) is another VGAM1081 host target gene. LOC219513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219513 BINDING SITE, designated SEQ ID:45296, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39479] Another function of VGAM1081 is therefore inhibition of LOC219513 (Accession XM_169166). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219513. LOC221641 (Accession XM_168090) is another VGAM1081 host target gene. LOC221641 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221641, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221641 BINDING SITE, designated SEQ ID:45009, to the nucleotide sequence of VGAM1081 RNA, herein designated VGAM RNA, also designated SEQ ID:3792.

[39480] Another function of VGAM1081 is therefore inhibition of LOC221641 (Accession XM_168090). Accordingly, utilities of VGAM1081 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221641. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1082 (VGAM1082) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39481] VGAM1082 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1082 was detected is described hereinabove with reference to Figs. 1-8.

[39482] VGAM1082 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diar-

rhea Virus. VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39483] VGAM1082 gene encodes a VGAM1082 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1082 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1082 precursor RNA is designated SEQ ID:1068, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1068 is located at position 15710 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39484] VGAM1082 precursor RNA folds onto itself, forming VGAM1082 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39485] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1082 folded precursor RNA into VGAM1082 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1082 RNA is designated SEQ ID:3793, and is provided hereinbelow with reference to the sequence listing part.

[39486] VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1082 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39487] VGAM1082 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1082 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1082 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39488] The complementary binding of VGAM1082 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1082 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1082 host target RNA into VGAM1082 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39489] It is appreciated that VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1082 host target genes. The mRNA of each one of this plurality of VGAM1082 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1082 RNA, herein designated VGAM RNA, and which when bound by VGAM1082 RNA causes inhibition of translation of respective one or more VGAM1082 host target proteins.

[39490] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1082 gene, herein designated VGAM GENE, on one or more VGAM1082 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39491] It is yet further appreciated that a function of VGAM1082 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1082 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1082 correlate with, and may be deduced from, the identity of the host target genes which VGAM1082 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39492] Nucleotide sequences of the VGAM1082 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1082 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1082 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1082 are further described hereinbelow with reference to Table 1.

[39493] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1082 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1082 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39494] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1082 gene, herein designated VGAM is inhibition of expression of VGAM1082 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1082 correlate with, and may be deduced from, the identity of the target genes which VGAM1082 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39495] Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459) is a VGAM1082 host target gene. SLC30A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC30A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC30A3 BINDING SITE,

designated SEQ ID:9529, to the nucleotide sequence of VGAM1082 RNA, herein designated VGAM RNA, also designated SEQ ID:3793.

[39496] A function of VGAM1082 is therefore inhibition of Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459). Accordingly, utilities of VGAM1082 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC30A3. FLJ20294 (Accession NM_017749) is another VGAM1082 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294 BINDING SITE, designated SEQ ID:19351, to the nucleotide sequence of VGAM1082 RNA, herein designated VGAM RNA, also designated SEQ ID:3793.

[39497] Another function of VGAM1082 is therefore inhibition of FLJ20294 (Accession NM_017749). Accordingly, utilities of VGAM1082 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20294. LOC149721 (Accession XM_086649) is another

VGAM1082 host target gene. LOC149721 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149721 BINDING SITE, designated SEQ ID:38812, to the nucleotide sequence of VGAM1082 RNA, herein designated VGAM RNA, also designated SEQ ID:3793.

[39498] Another function of VGAM1082 is therefore inhibition of LOC149721 (Accession XM_086649). Accordingly, utilities of VGAM1082 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149721. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1083 (VGAM1083) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39499] VGAM1083 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1083 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[39500] VGAM1083 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39501] VGAM1083 gene encodes a VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1083 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1083 precursor RNA is designated SEQ ID:1069, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1069 is located at position 13354 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39502] VGAM1083 precursor RNA folds onto itself, forming VGAM1083 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39503] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1083 folded precursor RNA into VGAM1083 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1083 RNA is designated SEQ ID:3794, and is provided hereinbelow with reference to the sequence listing part.

[39504] VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1083 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39505] VGAM1083 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1083 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1083 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1083 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39506] The complementary binding of VGAM1083 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1083 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1083 host target RNA into VGAM1083 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39507] It is appreciated that VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1083 host target genes. The mRNA of each one of this plurality of VGAM1083 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1083 RNA, herein designated VGAM RNA, and which when bound by VGAM1083 RNA causes inhibition of translation of respective one or more VGAM1083 host target proteins.

[39508] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1083 gene, herein designated VGAM GENE, on one or more VGAM1083 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39509] It is yet further appreciated that a function of VGAM1083 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1083 correlate with, and may be deduced from, the identity of the host target genes which VGAM1083 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39510] Nucleotide sequences of the VGAM1083 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1083 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1083 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1083 are further described hereinbelow with reference to Table 1.

[39511] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1083 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1083 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39512] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1083 gene, herein designated VGAM is inhibition of expression of VGAM1083 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1083 correlate with, and may be deduced from, the identity of the target genes which VGAM1083 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39513] HNF3G (Accession XM_051332) is a VGAM1083 host target gene. HNF3G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNF3G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HNF3G BINDING SITE, designated SEQ ID:35809, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39514] A function of VGAM1083 is therefore inhibition of HNF3G (Accession XM_051332). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNF3G. Lamin B Receptor (LBR, Accession XM_001795) is another VGAM1083 host target gene. LBR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBR BINDING SITE, designated SEQ ID:29855, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39515] Another function of VGAM1083 is therefore inhibition of Lamin B Receptor (LBR, Accession XM_001795). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with LBR. Myeloid Cell Leukemia Sequence 1 (BCL2-related) (MCL1, Accession NM_021960) is another VGAM1083 host target gene. MCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCL1 BINDING SITE, designated SEQ ID:22489, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39516] Another function of VGAM1083 is therefore inhibition of Myeloid Cell Leukemia Sequence 1 (BCL2-related) (MCL1, Accession NM_021960), a gene which involved in programming of differentiation and concomitant maintenance of viability. Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCL1. The function of MCL1 has been established by previous studies. Kozopas et al. (1993) isolated a gene, MCL1, from the ML-1 human myeloid leukemia cell line. Expression of MCL1 increased early in the induction, or programming, of differentiation in ML-1 (at 1-3 hr), before the appearance of differentia-

tion markers and mature morphology (at 1–3 days). MCL1 showed sequence similarity, particularly in the carboxyl portion, to BCL2 (OMIM Ref. No. 151430), a gene involved in normal lymphoid development and in lymphomas with the t(14;18) chromosome translocation. Further, in contrast to proliferation-associated oncogenes, the expression of MCL1 and BCL2 relates to the programming of differentiation/development and cell viability/death. Kozopas et al. (1993) suggested that MCL1 and BCL2 are 2 members of a 'new' gene family. Bae et al. (2000) identified a short splicing variant of MCL1, which they termed MCL1S. Sequence analysis indicated that the 271-amino acid variant lacks BCL2 homology domains 1 and 2 and the transmembrane domain due to the splicing out of exon 2 during mRNA processing. Unlike the full-length 350-amino acid MCL1 protein (MCL1L), yeast 2-hybrid analysis showed that MCL1S does not interact with proapoptotic BCL2 family proteins but dimerizes with the antiapoptotic MCL1L. Overexpression of MCL1S induced apoptosis in transfected CHO cells that could be antagonized by a caspase inhibitor or specifically by MCL1L. Therefore, the authors concluded that the fate of MCL1-expressing cells may be regulated through alterna-

tive splicing mechanisms and the interactions of the resulting gene products. Using the methods of somatic cell hybrid analysis and fluorescence in situ hybridization, Craig et al. (1994) mapped MCL1 to 1q21. In the mouse, MCL1-related sequences were mapped to positions on 2 mouse chromosomes, 3 and 5, using haplotype analysis of an interspecific cross. The locus on mouse chromosome 3, Mcl1, was homologous to MCL1 on human chromosome 1; the second locus, Mcl-rs, on mouse chromosome 5, may represent a pseudogene. The proximal long arm of human chromosome 1, where MCL1 is located, is duplicated and/or rearranged in a variety of preneoplastic and neoplastic diseases, including hematologic and solid tumors. Thus, MCL1 is a candidate gene for involvement in cancer. Animal model experiments lend further support to the function of MCL1. Rinkenberger et al. (2000) disrupted the Mcl1 locus in murine ES cells to determine the developmental roles of this Bcl2 family member. Deletion of Mcl1 resulted in periimplantation embryonic lethality. Homozygous Mcl1-deficient embryos did not implant in utero, but could be recovered at E3.5 to E4.0. Null blastocysts failed to hatch or attach in vitro, indicating a trophoblast defect, although the inner cell mass could

grow in culture. Of note, homozygous Mcl1-deficient blastocysts showed no evidence of increased apoptosis, but exhibited a delay in maturation beyond the precompaction stage. This model indicates that Mcl1 is essential for preimplantation development and implantation, and suggests that it has a function beyond regulating apoptosis.

[39517] It is appreciated that the abovementioned animal model for MCL1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[39518] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39519] Kozopas, K. M.; Yang, T.; Buchan, H. L.; Zhou, P.; Craig, R. W. : MCL1, a gene expressed in programmed myeloid cell differentiation, has sequence similarity to BCL2. Proc. Nat. Acad. Sci. 90: 3516–3520, 1993. ; and

[39520] Bae, J.; Leo, C. P.; Hsu, S. Y.; Hsueh, A. J. W. : MCL-1S, a splicing variant of the antiapoptotic BCL-2 family member MCL-1, encodes a proapoptotic protein possessing only the BH3 domain.

[39521] Further studies establishing the function and utilities of

MCL1 are found in John Hopkins OMIM database record ID 159552, and in cited publications numbered 3382–3385 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. T, Brachyury Homolog (mouse) (T, Accession NM_003181) is another VGAM1083 host target gene. T BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by T, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of T BINDING SITE, designated SEQ ID:9153, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39522] Another function of VGAM1083 is therefore inhibition of T, Brachyury Homolog (mouse) (T, Accession NM_003181), a gene which is a potent transcription factor. Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with T. The function of T has been established by previous studies. T protein is vital for the formation and differentiation of posterior mesoderm and for axial development in all vertebrates. Edwards et al. (1996) cited as evidence the

analysis of T mutant mice and zebrafish. 'Brachyury' mutant mice lack T protein and die in utero with abnormal notochord, absent somites, and reduced allantois. In zebrafish the 'no tail' mutation (ntl) is the homolog of 'Brachyury.' Ntl embryos die after hatching, lack notochords and tails, and possess abnormal trunk somites. The T gene encodes a transcription factor that binds to a specific DNA element via its N-terminal region. A protein motif within the DNA-binding domain, the so-called T box, is highly conserved among T homologs from different species and also defines a broader family of T-box genes; see TBX2 (OMIM Ref. No. 600747). Using the rat c-myc gene driven by a human metallothionein promoter, Abe et al. (2000) created several transgenic mouse lines. All of the males were sterile except those in line 137, indicating that the transgene is functionless in that line. However, most of the mice in line 137 had a kinked or bent tail. Abe et al. (2000) found that the transgene was integrated within intron 7 of the mouse Brachyury (T) gene and referred to the mutation as T-137, a null allele of the T gene. T-137 homozygotes showed an embryonic lethal phenotype. At embryonic day 9.5, fragmentation of the notochord was seen both anteriorly and posteriorly. At

embryonic day 10.5, the embryos tended to have an un-looped heart tube and a swollen pericardium cavity, indicating abnormality in heart function. The embryos died after embryonic day 10.5.

[39523] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39524] Abe, K.; Yamamura, K.; Suzuki, M. : Molecular and embryological characterization of a new transgene-induced null allele of mouse Brachyury locus. Mammalian Genome 11: 238–240, 2000. ; and

[39525] Edwards, Y. H.; Putt, W.; Lekoape, K. M.; Stott, D.; Fox, M.; Hopkinson, D. A.; Sowden, J. : The human homolog T of the mouse T (Brachyury) gene: gene structure, cDNA sequence, and ass.

[39526] Further studies establishing the function and utilities of T are found in John Hopkins OMIM database record ID 601397, and in cited publications numbered 648 and 6490–6495 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transglutaminase 4 (prostate) (TGM4, Accession NM_003241) is another VGAM1083 host target gene. TGM4 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by TGM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGM4 BINDING SITE, designated SEQ ID:9235, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39527] Another function of VGAM1083 is therefore inhibition of Transglutaminase 4 (prostate) (TGM4, Accession NM_003241), a gene which catalyzes the cross-linking of proteins and the conjugation of polyamines to specific proteins in the seminal tract. Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGM4. The function of TGM4 has been established by previous studies. In rodents, TGP is involved in the formation of copulatory plugs in the female genital tract after coitus, and may play a role in masking the antigenicity of the male gamete, thereby suppressing an immune response in the female genital tract against the sperm cells. By screening a human prostate library with a cDNA segment corresponding to the active-site region of TGC (TGM2), Dubbink et al. (1996) isolated a cDNA encoding human

TGP. The predicted 684-amino acid protein is 53% identical to rat TGP. In vitro translated human TGP has a molecular mass of approximately 77 kD. Northern blot analysis revealed that TGP is expressed as a 3.5-kb mRNA exclusively in prostate. Androgen induced TGP expression approximately 3-fold in a human prostate cancer cell line. Independently, Grant et al. (1994) cloned TGM4 cDNAs. They reported that the predicted protein contains 679 amino acids.

[39528] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39529] Dubbink, H. J.; Verkaik, N. S.; Faber, P. W.; Trapman, J.; Schroder, F. H.; Romijn, J. C. : Tissue-specific and androgen-regulated expression of human prostate-specific transglutaminase. *Biochem. J.* 315: 901-908, 1996. ; and

[39530] Grant, F. J.; Taylor, D. A.; Sheppard, P. O.; Mathewes, S. L.; Lint, W.; Vanaja, E.; Bishop, P. D.; O'Hara, P. J. : Molecular cloning and characterization of a novel transglutaminase cDN.

[39531] Further studies establishing the function and utilities of TGM4 are found in John Hopkins OMIM database record ID 600585, and in cited publications numbered

10212–10214 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM_003663) is another VGAM1083 host target gene. CGGBP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGGBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGGBP1 BINDING SITE, designated SEQ ID:9738, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39532] Another function of VGAM1083 is therefore inhibition of CGG Triplet Repeat Binding Protein 1 (CGGBP1, Accession NM_003663). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGGBP1. E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM_001421) is another VGAM1083 host target gene. ELF4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ELF4, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF4 BINDING SITE, designated SEQ ID:7127, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39533] Another function of VGAM1083 is therefore inhibition of E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM_001421). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF4. MGC4832 (Accession NM_145061) is another VGAM1083 host target gene. MGC4832 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4832 BINDING SITE, designated SEQ ID:29701, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39534] Another function of VGAM1083 is therefore inhibition of MGC4832 (Accession NM_145061). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC4832. Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM_005446) is another VGAM1083 host target gene. P2RXL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RXL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RXL1 BINDING SITE, designated SEQ ID:11931, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39535] Another function of VGAM1083 is therefore inhibition of Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM_005446). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RXL1. TRIP-Br2 (Accession NM_014755) is another VGAM1083 host target gene. TRIP-Br2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIP-Br2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16482, to the nucleotide sequence of VGAM1083 RNA, herein designated VGAM RNA, also designated SEQ ID:3794.

[39536] Another function of VGAM1083 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM1083 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1084 (VGAM1084) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39537] VGAM1084 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1084 was detected is described hereinabove with reference to Figs. 1-8.

[39538] VGAM1084 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[39539] VGAM1084 gene encodes a VGAM1084 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1084 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1084 precursor RNA is designated SEQ ID:1070, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1070 is located at position 11654 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39540] VGAM1084 precursor RNA folds onto itself, forming VGAM1084 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39541] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1084 folded precursor RNA into VGAM1084 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1084 RNA is designated SEQ ID:3795, and is provided hereinbelow with reference to the sequence listing part.

[39542] VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1084 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39543] VGAM1084 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1084 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1084 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39544] The complementary binding of VGAM1084 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1084 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1084 host target RNA into VGAM1084 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39545] It is appreciated that VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1084 host target genes. The mRNA of each one of this plurality of VGAM1084 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1084 RNA, herein designated VGAM RNA, and which when bound by VGAM1084 RNA causes inhibition of translation of respective one or more VGAM1084 host target proteins.

[39546] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1084 gene, herein designated VGAM GENE, on one or more VGAM1084 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39547] It is yet further appreciated that a function of VGAM1084 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1084 correlate with, and may be deduced from, the identity of the host target genes which VGAM1084 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39548] Nucleotide sequences of the VGAM1084 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1084 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1084 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1084 are further described hereinbelow with reference to Table 1.

[39549] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1084 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1084 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39550] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1084 gene, herein designated VGAM is inhibition of expression of VGAM1084 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1084 correlate with, and may be deduced from, the identity of the target genes which VGAM1084 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39551] Fibromodulin (FMOD, Accession NM_002023) is a VGAM1084 host target gene. FMOD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMOD BINDING SITE, designated SEQ ID:7773, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39552] A function of VGAM1084 is therefore inhibition of Fibro-modulin (FMOD, Accession NM_002023), a gene which affects the rate of fibrils formation. Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMOD. The function of FMOD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM39. Ribonuclease/angiogenin Inhibitor (RNH, Accession NM_002939) is another VGAM1084 host target gene. RNH BINDING SITE1 and RNH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RNH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNH BINDING SITE1 and RNH BINDING SITE2, designated SEQ ID:8846 and SEQ ID:29995 respectively, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39553] Another function of VGAM1084 is therefore inhibition of Ribonuclease/angiogenin Inhibitor (RNH, Accession NM_002939), a gene which is an inhibitor of pancreatic

rnase and angiogenin. may also function in the modulation of cellular activities. Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNH. The function of RNH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM484. ELKS (Accession NM_015064) is another VGAM1084 host target gene. ELKS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELKS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELKS BINDING SITE, designated SEQ ID:17418, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39554] Another function of VGAM1084 is therefore inhibition of ELKS (Accession NM_015064). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELKS. FLJ22313 (Accession NM_022373) is another VGAM1084 host target gene. FLJ22313 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by FLJ22313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22313 BINDING SITE, designated SEQ ID:22761, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39555] Another function of VGAM1084 is therefore inhibition of FLJ22313 (Accession NM_022373). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22313. FLJ23519 (Accession XM_044932) is another VGAM1084 host target gene. FLJ23519 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23519 BINDING SITE, designated SEQ ID:34309, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39556] Another function of VGAM1084 is therefore inhibition of

FLJ23519 (Accession XM_044932). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23519. MGC4309 (Accession NM_024115) is another VGAM1084 host target gene. MGC4309 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4309, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4309 BINDING SITE, designated SEQ ID:23567, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39557] Another function of VGAM1084 is therefore inhibition of MGC4309 (Accession NM_024115). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4309. Zinc Finger Protein 33a (KOX 31) (ZNF33A, Accession XM_166119) is another VGAM1084 host target gene. ZNF33A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF33A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of ZNF33A BINDING SITE, designated SEQ ID:43897, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39558] Another function of VGAM1084 is therefore inhibition of Zinc Finger Protein 33a (KOX 31) (ZNF33A, Accession XM_166119). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF33A. LOC152503 (Accession XM_098238) is another VGAM1084 host target gene. LOC152503 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152503 BINDING SITE, designated SEQ ID:41517, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39559] Another function of VGAM1084 is therefore inhibition of LOC152503 (Accession XM_098238). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152503. LOC51236 (Accession NM_016458) is another VGAM1084 host target gene. LOC51236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51236 BINDING SITE, designated SEQ ID:18569, to the nucleotide sequence of VGAM1084 RNA, herein designated VGAM RNA, also designated SEQ ID:3795.

[39560] Another function of VGAM1084 is therefore inhibition of LOC51236 (Accession NM_016458). Accordingly, utilities of VGAM1084 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51236. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1085 (VGAM1085) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39561] VGAM1085 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1085 was detected is described hereinabove with reference to Figs. 1–8.

[39562] VGAM1085 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39563] VGAM1085 gene encodes a VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1085 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1085 precursor RNA is designated SEQ ID:1071, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1071 is located at position 14382 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39564] VGAM1085 precursor RNA folds onto itself, forming VGAM1085 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39565] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1085 folded precursor RNA into VGAM1085 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1085 RNA is designated SEQ ID:3796, and is provided hereinbelow with reference to the sequence listing part.

[39566] VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1085 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39567] VGAM1085 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1085 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1085 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39568] The complementary binding of VGAM1085 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1085 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1085 host target RNA into VGAM1085 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39569] It is appreciated that VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1085 host target genes. The mRNA of each one of this plurality of VGAM1085 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1085 RNA, herein designated VGAM RNA, and which when bound by VGAM1085 RNA causes inhibition of translation of respective one or more VGAM1085 host target proteins.

[39570] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1085 gene, herein designated VGAM GENE, on one or more VGAM1085 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39571] It is yet further appreciated that a function of VGAM1085 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1085 correlate with, and may be deduced from, the identity of the host target genes which VGAM1085 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39572] Nucleotide sequences of the VGAM1085 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1085 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1085 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1085 are further described hereinbelow with reference to Table 1.

[39573] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1085 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1085 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39574] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1085 gene, herein designated VGAM is inhibition of expression of VGAM1085 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1085 correlate with, and may be deduced from, the identity of the target genes which VGAM1085 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39575] HCS (Accession NM_018947) is a VGAM1085 host target gene. HCS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

HCS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCS BINDING SITE, designated SEQ ID:21015, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39576] A function of VGAM1085 is therefore inhibition of HCS (Accession NM_018947). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCS. FLJ11164 (Accession NM_018346) is another VGAM1085 host target gene. FLJ11164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11164 BINDING SITE, designated SEQ ID:20356, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39577] Another function of VGAM1085 is therefore inhibition of FLJ11164 (Accession NM_018346). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ11164. Mitogen-activated Protein Kinase-activated Protein Kinase 3 (MAPKAPK3, Accession NM_004635) is another VGAM1085 host target gene. MAPKAPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPKAPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPKAPK3 BINDING SITE, designated SEQ ID:11011, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39578] Another function of VGAM1085 is therefore inhibition of Mitogen-activated Protein Kinase-activated Protein Kinase 3 (MAPKAPK3, Accession NM_004635). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPKAPK3. SE57-1 (Accession NM_025214) is another VGAM1085 host target gene. SE57-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SE57-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SE57-1 BINDING SITE, designated SEQ ID:24892, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39579] Another function of VGAM1085 is therefore inhibition of SE57-1 (Accession NM_025214). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SE57-1. LOC143920 (Accession XM_084658) is another VGAM1085 host target gene. LOC143920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143920 BINDING SITE, designated SEQ ID:37638, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39580] Another function of VGAM1085 is therefore inhibition of LOC143920 (Accession XM_084658). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143920. LOC157317 (Accession XM_088293) is an-

other VGAM1085 host target gene. LOC157317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157317 BINDING SITE, designated SEQ ID:39585, to the nucleotide sequence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39581] Another function of VGAM1085 is therefore inhibition of LOC157317 (Accession XM_088293). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157317. LOC203429 (Accession XM_114701) is another VGAM1085 host target gene. LOC203429 BINDING SITE1 and LOC203429 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC203429, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203429 BINDING SITE1 and LOC203429 BINDING SITE2, designated SEQ ID:43049 and SEQ ID:43050 respectively, to the nucleotide se-

quence of VGAM1085 RNA, herein designated VGAM RNA, also designated SEQ ID:3796.

[39582] Another function of VGAM1085 is therefore inhibition of LOC203429 (Accession XM_114701). Accordingly, utilities of VGAM1085 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203429. CBCIP2 (Accession NM_032831) is another VGAM1086 host target gene. CBCIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBCIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBCIP2 BINDING SITE, designated SEQ ID:26606, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39583] Another function of VGAM1086 is therefore inhibition of CBCIP2 (Accession NM_032831). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBCIP2. Cyclin M1 (CNNM1, Accession NM_020348) is another VGAM1086 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21604, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39584] Another function of VGAM1086 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM_020348). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. FLJ00024 (Accession XM_033361) is another VGAM1086 host target gene. FLJ00024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00024 BINDING SITE, designated SEQ ID:31897, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39585] Another function of VGAM1086 is therefore inhibition of FLJ00024 (Accession XM_033361). Accordingly, utilities of

VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00024. FLJ13984 (Accession NM_024770) is another VGAM1086 host target gene. FLJ13984 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13984, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13984 BINDING SITE, designated SEQ ID:24130, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39586] Another function of VGAM1086 is therefore inhibition of FLJ13984 (Accession NM_024770). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13984. LOC196485 (Accession XM_113731) is another VGAM1086 host target gene. LOC196485 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC196485 BINDING SITE, designated SEQ ID:42382, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39587] Another function of VGAM1086 is therefore inhibition of LOC196485 (Accession XM_113731). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196485. LOC202986 (Accession XM_117489) is another VGAM1086 host target gene. LOC202986 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202986 BINDING SITE, designated SEQ ID:43473, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39588] Another function of VGAM1086 is therefore inhibition of LOC202986 (Accession XM_117489). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202986. LOC221354 (Accession XM_166468) is another VGAM1086 host target gene. LOC221354 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221354 BINDING SITE, designated SEQ ID:44393, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39589] Another function of VGAM1086 is therefore inhibition of LOC221354 (Accession XM_166468). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221354. LOC90333 (Accession XM_030958) is another VGAM1086 host target gene. LOC90333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90333 BINDING SITE, designated SEQ ID:31219, to the nucleotide sequence of VGAM1086 RNA, herein designated VGAM RNA, also designated SEQ ID:3797.

[39590] Another function of VGAM1086 is therefore inhibition of

LOC90333 (Accession XM_030958). Accordingly, utilities of VGAM1086 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1087 (VGAM1087) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39591] VGAM1087 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1087 was detected is described hereinabove with reference to Figs. 1-8.

[39592] VGAM1087 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39593] VGAM1087 gene encodes a VGAM1087 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1087 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1087 precursor RNA is designated SEQ ID:1073, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1073 is located at position 5802 relative to the genome of Porcine Epidemic Diarrhea Virus.

- [39594] VGAM1087 precursor RNA folds onto itself, forming VGAM1087 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39595] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1087 folded precursor RNA into VGAM1087 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM1087 RNA is designated SEQ ID:3798, and is provided hereinbelow with reference to the sequence listing part.

[39596] VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1087 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39597] VGAM1087 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1087 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1087 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39598] The complementary binding of VGAM1087 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1087 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1087 host target RNA into VGAM1087 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39599] It is appreciated that VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1087 host target genes. The mRNA of each one of this plurality of VGAM1087 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1087 RNA, herein designated VGAM RNA, and which when bound by VGAM1087 RNA causes inhibition of translation of respective one or more VGAM1087 host target proteins.

[39600] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1087 gene, herein designated VGAM GENE, on one or more VGAM1087 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39601] It is yet further appreciated that a function of VGAM1087

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1087 correlate with, and may be deduced from, the identity of the host target genes which VGAM1087 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39602] Nucleotide sequences of the VGAM1087 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1087 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1087 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1087 are further described hereinbelow with reference to Table 1.

[39603] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1087 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1087 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39604] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1087 gene, herein designated VGAM is inhibition of expression of VGAM1087 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1087 correlate with, and may be deduced from, the identity of the target genes which VGAM1087 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39605] PAG (Accession NM_018440) is a VGAM1087 host target gene. PAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAG BINDING SITE, designated SEQ ID:20509, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39606] A function of VGAM1087 is therefore inhibition of PAG (Accession NM_018440). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAG. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768) is another VGAM1087 host target gene.

PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9848, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39607] Another function of VGAM1087 is therefore inhibition of Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768), a gene which is a phosphoprotein and involved in glucose uptake. Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949.Xeroderma Pigmentosum, Complementation Group C (XPC, Accession NM_004628) is another VGAM1087 host target gene. XPC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XPC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XPC BINDING SITE, designated SEQ ID:10999, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39608] Another function of VGAM1087 is therefore inhibition of Xeroderma Pigmentosum, Complementation Group C (XPC, Accession NM_004628). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XPC. Bromodomain Containing 3 (BRD3, Accession NM_007371) is another VGAM1087 host target gene. BRD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRD3 BINDING SITE, designated SEQ ID:14297, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39609] Another function of VGAM1087 is therefore inhibition of Bromodomain Containing 3 (BRD3, Accession NM_007371). Accordingly, utilities of VGAM1087 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD3. Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM_114191) is another VGAM1087 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ ID:42766, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39610] Another function of VGAM1087 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM_114191). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. FLJ22965 (Accession NM_022101) is another VGAM1087 host target gene. FLJ22965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22965 BINDING SITE, designated SEQ ID:22644, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39611] Another function of VGAM1087 is therefore inhibition of FLJ22965 (Accession NM_022101). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22965. KIAA0895 (Accession XM_166573) is another VGAM1087 host target gene. KIAA0895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0895 BINDING SITE, designated SEQ ID:44546, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39612] Another function of VGAM1087 is therefore inhibition of KIAA0895 (Accession XM_166573). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0895. KIAA1305 (Accession NM_025081) is another VGAM1087 host target gene. KIAA1305 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1305 BINDING SITE, designated SEQ ID:24681, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39613] Another function of VGAM1087 is therefore inhibition of KIAA1305 (Accession NM_025081). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1305. MGC4737 (Accession NM_031466) is another VGAM1087 host target gene. MGC4737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4737 BINDING SITE, designated SEQ ID:25505, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM

RNA, also designated SEQ ID:3798.

[39614] Another function of VGAM1087 is therefore inhibition of MGC4737 (Accession NM_031466). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4737. LOC163812 (Accession XM_089158) is another VGAM1087 host target gene. LOC163812 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163812 BINDING SITE, designated SEQ ID:39967, to the nucleotide sequence of VGAM1087 RNA, herein designated VGAM RNA, also designated SEQ ID:3798.

[39615] Another function of VGAM1087 is therefore inhibition of LOC163812 (Accession XM_089158). Accordingly, utilities of VGAM1087 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163812. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1088 (VGAM1088) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39616] VGAM1088 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1088 was detected is described hereinabove with reference to Figs. 1–8.

[39617] VGAM1088 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39618] VGAM1088 gene encodes a VGAM1088 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1088 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1088 precursor RNA is designated SEQ ID:1074, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1074 is located at position 1913 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39619] VGAM1088 precursor RNA folds onto itself, forming

VGAM1088 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39620] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1088 folded precursor RNA into VGAM1088 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1088 RNA is designated SEQ ID:3799, and is provided hereinbelow with reference to the sequence listing part.

[39621] VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1088 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39622] VGAM1088 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1088 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1088 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39623] The complementary binding of VGAM1088 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1088 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1088 host target RNA into VGAM1088 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39624] It is appreciated that VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1088 host target genes. The mRNA of each one of this plurality of VGAM1088 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1088 RNA, herein designated VGAM RNA, and which when bound by VGAM1088 RNA causes inhibition of translation of respective one or more VGAM1088 host target proteins.

[39625] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1088 gene, herein designated VGAM GENE, on one or more VGAM1088 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39626] It is yet further appreciated that a function of VGAM1088 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1088 correlate with, and may be deduced from, the identity of the host target genes which VGAM1088 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39627] Nucleotide sequences of the VGAM1088 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1088 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1088 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1088 are further described hereinbelow with reference to Table 1.

[39628] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1088 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1088 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39629] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1088 gene, herein designated VGAM is inhibition of expression of VGAM1088 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1088 correlate with, and may be deduced from, the identity of the target genes which VGAM1088 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[39630] Cytotoxic T-lymphocyte-associated Protein 4 (CTLA4, Accession NM_005214) is a VGAM1088 host target gene. CTLA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTLA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTLA4 BINDING SITE, designated SEQ ID:11711, to the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, also designated SEQ ID:3799.

[39631] A function of VGAM1088 is therefore inhibition of Cytotoxic T-lymphocyte-associated Protein 4 (CTLA4, Accession NM_005214). Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTLA4. Neuronal Cell Adhesion Molecule (NRCAM, Accession NM_005010) is another VGAM1088 host target gene. NRCAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRCAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of NRCAM BINDING SITE, designated SEQ ID:11448, to the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, also designated SEQ ID:3799.

[39632] Another function of VGAM1088 is therefore inhibition of Neuronal Cell Adhesion Molecule (NRCAM, Accession NM_005010), a gene which functions as a cell surface protein and belongs to the immunoglobulin superfamily. Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRCAM. The function of NRCAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM268.FLJ21432 (Accession NM_024551) is another VGAM1088 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23766, to the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, also designated SEQ

ID:3799.

[39633] Another function of VGAM1088 is therefore inhibition of FLJ21432 (Accession NM_024551). Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. PP1628 (Accession NM_025201) is another VGAM1088 host target gene. PP1628 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PP1628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1628 BINDING SITE, designated SEQ ID:24857, to the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, also designated SEQ ID:3799.

[39634] Another function of VGAM1088 is therefore inhibition of PP1628 (Accession NM_025201). Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1628. LOC159199 (Accession XM_089441) is another VGAM1088 host target gene. LOC159199 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC159199, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159199 BINDING SITE, designated SEQ ID:39979, to the nucleotide sequence of VGAM1088 RNA, herein designated VGAM RNA, also designated SEQ ID:3799.

[39635] Another function of VGAM1088 is therefore inhibition of LOC159199 (Accession XM_089441). Accordingly, utilities of VGAM1088 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159199. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1089 (VGAM1089) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39636] VGAM1089 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1089 was detected is described hereinabove with reference to Figs. 1-8.

[39637] VGAM1089 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diar-

rhea Virus. VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39638] VGAM1089 gene encodes a VGAM1089 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1089 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1089 precursor RNA is designated SEQ ID:1075, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1075 is located at position 3305 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39639] VGAM1089 precursor RNA folds onto itself, forming VGAM1089 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39640] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1089 folded precursor RNA into VGAM1089 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1089 RNA is designated SEQ ID:3800, and is provided hereinbelow with reference to the sequence listing part.

[39641] VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1089 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39642] VGAM1089 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1089 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1089 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39643] The complementary binding of VGAM1089 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1089 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1089 host target RNA into VGAM1089 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39644] It is appreciated that VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1089 host target genes. The mRNA of each one of this plurality of VGAM1089 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1089 RNA, herein designated VGAM RNA, and which when bound by VGAM1089 RNA causes inhibition of translation of respective one or more VGAM1089 host target proteins.

[39645] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1089 gene, herein designated VGAM GENE, on one or more VGAM1089 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39646] It is yet further appreciated that a function of VGAM1089 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1089 correlate with, and may be deduced from, the identity of the host target genes which VGAM1089 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39647] Nucleotide sequences of the VGAM1089 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1089 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1089 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1089 are further described hereinbelow with reference to Table 1.

[39648] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1089 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1089 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39649] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1089 gene, herein designated VGAM is inhibition of expression of VGAM1089 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1089 correlate with, and may be deduced from, the identity of the target genes which VGAM1089 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39650] Hyaluronan Synthase 3 (HAS3, Accession NM_005329) is a VGAM1089 host target gene. HAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAS3 BINDING SITE, designated SEQ ID:11802, to the nucleotide sequence of

VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39651] A function of VGAM1089 is therefore inhibition of Hyaluronan Synthase 3 (HAS3, Accession NM_005329), a gene which plays a role in hyaluronan/hyaluronic acid (ha) synthesis. Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAS3. The function of HAS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM498. Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945) is another VGAM1089 host target gene. C21orf25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf25 BINDING SITE, designated SEQ ID:31796, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39652] Another function of VGAM1089 is therefore inhibition of

Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf25. ERG-1 (Accession NM_022034) is another VGAM1089 host target gene. ERG-1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ERG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERG-1 BINDING SITE, designated SEQ ID:22557, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39653] Another function of VGAM1089 is therefore inhibition of ERG-1 (Accession NM_022034). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERG-1. FLJ13590 (Accession NM_024840) is another VGAM1089 host target gene. FLJ13590 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13590, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13590 BINDING SITE, designated SEQ ID:24250, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39654] Another function of VGAM1089 is therefore inhibition of FLJ13590 (Accession NM_024840). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13590. FLJ14810 (Accession NM_032843) is another VGAM1089 host target gene. FLJ14810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14810 BINDING SITE, designated SEQ ID:26632, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39655] Another function of VGAM1089 is therefore inhibition of FLJ14810 (Accession NM_032843). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ14810. Internexin Neuronal Intermediate Filament Protein, Alpha (INA, Accession NM_032727) is another VGAM1089 host target gene. INA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by INA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INA BINDING SITE, designated SEQ ID:26454, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39656] Another function of VGAM1089 is therefore inhibition of Internexin Neuronal Intermediate Filament Protein, Alpha (INA, Accession NM_032727). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INA. INSM2 (Accession NM_032594) is another VGAM1089 host target gene. INSM2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by INSM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INSM2 BINDING SITE, designated SEQ

ID:26326, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39657] Another function of VGAM1089 is therefore inhibition of INSM2 (Accession NM_032594). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INSM2. KIAA0261 (Accession XM_042946) is another VGAM1089 host target gene. KIAA0261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0261 BINDING SITE, designated SEQ ID:33830, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39658] Another function of VGAM1089 is therefore inhibition of KIAA0261 (Accession XM_042946). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0261. KIAA1483 (Accession XM_045920) is another VGAM1089 host target gene. KIAA1483 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1483 BINDING SITE, designated SEQ ID:34617, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39659] Another function of VGAM1089 is therefore inhibition of KIAA1483 (Accession XM_045920). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1483. KIAA1530 (Accession XM_042661) is another VGAM1089 host target gene. KIAA1530 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1530, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1530 BINDING SITE, designated SEQ ID:33737, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39660] Another function of VGAM1089 is therefore inhibition of

KIAA1530 (Accession XM_042661). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1530. Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622) is another VGAM1089 host target gene. MRPL35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL35 BINDING SITE, designated SEQ ID:18733, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39661] Another function of VGAM1089 is therefore inhibition of Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL35. N-ethylmaleimide-sensitive Factor Attachment Protein, Gamma (NAPG, Accession XM_172983) is another VGAM1089 host target gene. NAPG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by NAPG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAPG BINDING SITE, designated SEQ ID:46251, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39662] Another function of VGAM1089 is therefore inhibition of N-ethylmaleimide-sensitive Factor Attachment Protein, Gamma (NAPG, Accession XM_172983). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAPG. Solute Carrier Family 26 (sulfate transporter), Member 1 (SLC26A1, Accession NM_022042) is another VGAM1089 host target gene. SLC26A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC26A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A1 BINDING SITE, designated SEQ ID:22567, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39663] Another function of VGAM1089 is therefore inhibition of Solute Carrier Family 26 (sulfate transporter), Member 1 (SLC26A1, Accession NM_022042). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A1. Serine/threonine Kinase 29 (STK29, Accession XM_113646) is another VGAM1089 host target gene. STK29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK29 BINDING SITE, designated SEQ ID:42317, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39664] Another function of VGAM1089 is therefore inhibition of Serine/threonine Kinase 29 (STK29, Accession XM_113646). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK29. LOC162165 (Accession XM_102442) is another VGAM1089 host target gene. LOC162165 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by LOC162165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162165 BINDING SITE, designated SEQ ID:42117, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39665] Another function of VGAM1089 is therefore inhibition of LOC162165 (Accession XM_102442). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162165. LOC196527 (Accession XM_113743) is another VGAM1089 host target gene. LOC196527 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196527 BINDING SITE, designated SEQ ID:42400, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39666] Another function of VGAM1089 is therefore inhibition of

LOC196527 (Accession XM_113743). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196527. LOC221002 (Accession XM_166156) is another VGAM1089 host target gene. LOC221002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221002 BINDING SITE, designated SEQ ID:43972, to the nucleotide sequence of VGAM1089 RNA, herein designated VGAM RNA, also designated SEQ ID:3800.

[39667] Another function of VGAM1089 is therefore inhibition of LOC221002 (Accession XM_166156). Accordingly, utilities of VGAM1089 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221002. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1090 (VGAM1090) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[39668] VGAM1090 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1090 was detected is described hereinabove with reference to Figs. 1–8.

[39669] VGAM1090 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Epidemic Diarrhea Virus. VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39670] VGAM1090 gene encodes a VGAM1090 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1090 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1090 precursor RNA is designated SEQ ID:1076, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1076 is located at position 2399 relative to the genome of Porcine Epidemic Diarrhea Virus.

[39671] VGAM1090 precursor RNA folds onto itself, forming VGAM1090 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39672] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1090 folded precursor RNA into VGAM1090 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1090 RNA is designated SEQ ID:3801, and is provided hereinbelow with reference to the sequence listing part.

[39673] VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1090 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[39674] VGAM1090 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1090 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1090 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[39675] The complementary binding of VGAM1090 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1090 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1090 host target RNA into VGAM1090 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39676] It is appreciated that VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1090 host target genes. The mRNA of each one of this plurality of VGAM1090 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1090 RNA, herein designated VGAM RNA, and which when bound by VGAM1090 RNA causes inhibition of translation of respective one or more VGAM1090 host target proteins.

[39677] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1090 gene, herein designated VGAM GENE, on one

or more VGAM1090 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39678] It is yet further appreciated that a function of VGAM1090 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGAM1090 correlate with, and may be deduced from, the identity of the host target genes which VGAM1090 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39679] Nucleotide sequences of the VGAM1090 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1090 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1090 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1090 are further described hereinbelow with reference to Table 1.

[39680] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1090 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1090 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39681] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1090 gene, herein designated VGAM is inhibition of expression of VGAM1090 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1090 correlate with, and may be deduced from, the identity of the target genes which VGAM1090 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39682] B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A,

Accession NM_018014) is a VGAM1090 host target gene. BCL11A BINDING SITE1 and BCL11A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BCL11A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL11A BINDING SITE1 and BCL11A BINDING SITE2, designated SEQ ID:19752 and SEQ ID:28852 respectively, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39683] A function of VGAM1090 is therefore inhibition of B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A, Accession NM_018014), a gene which acts as a transcriptional repressor. Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11A. The function of BCL11A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM190.SWAP70 (Accession XM_049197) is another VGAM1090 host target gene. SWAP70 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SWAP70, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SWAP70 BINDING SITE, designated SEQ ID:35346, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39684] Another function of VGAM1090 is therefore inhibition of SWAP70 (Accession XM_049197), a gene which is involved not only in nuclear events but also in signaling in B-cell activation. Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SWAP70. The function of SWAP70 has been established by previous studies. The B-cell receptor is composed of the immunoglobulin (Ig) heavy and light chains and the covalently bound accessory molecules Ig-alpha (CD79A; 112205) and Ig-beta (CD79B; 147245). Crosslinking of the B-cell receptor by antigens stimulates the activation of intracellular protein kinases. B-cell activation leads to hypermutation of the Ig variable regions and to heavy chain class switching, in which the Ig constant region of mu (IgM; OMIM Ref. No. 147020) is replaced by that of another class: gamma (IgG; OMIM Ref.

No. 147100), alpha (IgA; OMIM Ref. No. 146900), or epsilon (IgE; OMIM Ref. No. 147180). Class switching is achieved by a looping out and deletion mechanism between the switch region of mu and the switch region of the isotype that is to be expressed. Masat et al. (2000) explored the possibility that switch-associated protein-70 (OMIM Ref. No. SWAP70) acts as a link between the recognition of specific switch regions and causation of a DNA break. Swap70 had been isolated in the mouse as part of a complex that is able to promote recombination between 2 switch regions in vitro (Borggreffe et al., 1998; Borggreffe et al., 1999). By screening a human lymphoma cDNA library using mouse Swap70 sequences as the probe, Masat et al. (2000) isolated a cDNA encoding SWAP70. Although the 585-amino acid SWAP70 protein contains 3 nuclear localization signals, SWAP70 was found mainly in the cytoplasm in small resting B cells. On stimulation, SWAP70 translocated to the nucleus. In activated, class-switching B cell cultures, it was associated with membrane IgG, but not IgM. Masat et al. (2000) suggested that SWAP70 is involved not only in nuclear events but also in signaling in B-cell activation. Shinohara et al. (2002) demonstrated that SWAP70 specifically binds phosphatidylinositol-

3,4,5-triphosphate. On stimulation by growth factors, cytoplasmic SWAP70, which is dependent on phosphoinositide-3-hydroxykinase but independent of Ras (see OMIM Ref. No. 190020), moved to cell membrane rearrangements known as ruffles. However, mutant SWAP70 lacking the ability to bind phosphatidylinositol-

3,4,5-triphosphate blocked membrane ruffling induced by epidermal growth factor (EGF; 131530) or platelet-derived growth factor (see OMIM Ref. No. 173430). SWAP70 shows low homology with Rac-guanine nucleotide exchange factors, and catalyzes phosphatidylinositol-

3,4,5-triphosphate-dependent guanine nucleotide exchange to Rac (see OMIM Ref. No. 602048).

SWAP70-deficient fibroblasts showed impaired membrane ruffling after stimulation with EGF, and failed to activate Rac fully. Shinohara et al. (2002) concluded that SWAP70 is a different type of Rac-GEF which, independently of Ras, transduces signals from tyrosine kinase receptors to Rac.

[39685] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39686] Masat, L.; Caldwell, J.; Armstrong, R.; Khoshnevisan, H.; Jessberger, R.; Herndier, B.; Wabl, M.; Ferrick, D. : Associ-

ation of SWAP-70 with the B cell antigen receptor complex. Proc. Nat. Acad. Sci. 97: 2180-2184, 2000. ; and

[39687] Shinohara, M.; Terada, Y.; Iwamatsu, A.; Shinohara, A.; Mochizuki, N.; Higuchi, M.; Gotoh, Y.; Ihara, S.; Nagata, S.; Itoh, H.; Fukui, Y.; Jessberger, R. : SWAP-70 is a guanine-nucleot.

[39688] Further studies establishing the function and utilities of SWAP70 are found in John Hopkins OMIM database record ID 604762, and in cited publications numbered 7286-7290 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adenylate Kinase 5 (AK5, Accession NM_012093) is another VGAM1090 host target gene. AK5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK5 BINDING SITE, designated SEQ ID:14394, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39689] Another function of VGAM1090 is therefore inhibition of Adenylate Kinase 5 (AK5, Accession NM_012093). Accord-

ingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK5. CHRNA7 (cholinergic receptor, nicotinic, alpha polypeptide 7, exons 5–10) and FAM7A (family with sequence similarity 7A, exons A–E) Fusion (CHRFAM7A, Accession XM_170784) is another VGAM1090 host target gene. CHRFAM7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRFAM7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRFAM7A BINDING SITE, designated SEQ ID:45553, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39690] Another function of VGAM1090 is therefore inhibition of CHRNA7 (cholinergic receptor, nicotinic, alpha polypeptide 7, exons 5–10) and FAM7A (family with sequence similarity 7A, exons A–E) Fusion (CHRFAM7A, Accession XM_170784). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRFAM7A. FLJ13215 (Accession NM_025004) is another VGAM1090 host target

gene. FLJ13215 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13215 BINDING SITE, designated SEQ ID:24576, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39691] Another function of VGAM1090 is therefore inhibition of FLJ13215 (Accession NM_025004). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13215. KIAA1430 (Accession XM_087593) is another VGAM1090 host target gene. KIAA1430 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1430 BINDING SITE, designated SEQ ID:39357, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39692] Another function of VGAM1090 is therefore inhibition of KIAA1430 (Accession XM_087593). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1430. PRO2955 (Accession NM_018545) is another VGAM1090 host target gene. PRO2955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2955 BINDING SITE, designated SEQ ID:20620, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39693] Another function of VGAM1090 is therefore inhibition of PRO2955 (Accession NM_018545). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2955. LOC148014 (Accession XM_085999) is another VGAM1090 host target gene. LOC148014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148014, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148014 BINDING SITE, designated SEQ ID:38442, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39694] Another function of VGAM1090 is therefore inhibition of LOC148014 (Accession XM_085999). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148014. LOC90917 (Accession XM_034861) is another VGAM1090 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32165, to the nucleotide sequence of VGAM1090 RNA, herein designated VGAM RNA, also designated SEQ ID:3801.

[39695] Another function of VGAM1090 is therefore inhibition of LOC90917 (Accession XM_034861). Accordingly, utilities of VGAM1090 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90917. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1091 (VGAM1091) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39696] VGAM1091 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1091 was detected is described hereinabove with reference to Figs. 1–8.

[39697] VGAM1091 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Poinsettia Mosaic Virus. VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39698] VGAM1091 gene encodes a VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1091 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1091 precursor RNA is designated SEQ ID:1077, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1077 is located at position 854 relative to the genome of Poinsettia Mosaic Virus.

- [39699] VGAM1091 precursor RNA folds onto itself, forming VGAM1091 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39700] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1091 folded precursor RNA into VGAM1091 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1091 RNA is designated SEQ ID:3802, and is provided hereinbelow with reference to the sequence listing part.

[39701] VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1091 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39702] VGAM1091 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1091 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1091 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39703] The complementary binding of VGAM1091 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1091 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1091 host target RNA into VGAM1091 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39704] It is appreciated that VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1091 host target genes. The mRNA of each one of this plurality of VGAM1091 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1091 RNA, herein designated VGAM RNA, and which when bound by VGAM1091 RNA causes

inhibition of translation of respective one or more VGAM1091 host target proteins.

[39705] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1091 gene, herein designated VGAM GENE, on one or more VGAM1091 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39706] It is yet further appreciated that a function of VGAM1091 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1091 include diagnosis, prevention and

treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1091 correlate with, and may be deduced from, the identity of the host target genes which VGAM1091 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39707] Nucleotide sequences of the VGAM1091 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1091 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1091 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1091 are further described hereinbelow with reference to Table 1.

[39708] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1091 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1091 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39709] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1091 gene, herein designated VGAM is inhibition of expression of VGAM1091 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1091 correlate with, and may be deduced from, the identity of the target genes which VGAM1091 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39710] MGC13057 (Accession NM_032321) is a VGAM1091 host target gene. MGC13057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13057 BINDING SITE, designated SEQ ID:26125, to the nucleotide sequence of VGAM1091 RNA, herein designated VGAM RNA, also designated SEQ ID:3802.

[39711] A function of VGAM1091 is therefore inhibition of MGC13057 (Accession NM_032321). Accordingly, utilities of VGAM1091 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13057. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1092 (VGAM1092) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39712] VGAM1092 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1092 was detected is described hereinabove with reference to Figs. 1–8.

[39713] VGAM1092 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Poinsettia Mosaic Virus. VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39714] VGAM1092 gene encodes a VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1092 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1092 precursor RNA is designated SEQ ID:1078, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1078 is located at position 92 relative to the genome of Poinsettia Mosaic Virus.

[39715] VGAM1092 precursor RNA folds onto itself, forming

VGAM1092 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39716] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1092 folded precursor RNA into VGAM1092 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1092 RNA is designated SEQ ID:3803, and is provided hereinbelow with reference to the sequence listing part.

[39717] VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1092 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39718] VGAM1092 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1092 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1092 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39719] The complementary binding of VGAM1092 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1092 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1092 host target RNA into VGAM1092 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39720] It is appreciated that VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1092 host target genes. The mRNA of each one of this plurality of VGAM1092 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1092 RNA, herein designated VGAM RNA, and which when bound by VGAM1092 RNA causes inhibition of translation of respective one or more VGAM1092 host target proteins.

[39721] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1092 gene, herein designated VGAM GENE, on one or more VGAM1092 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39722] It is yet further appreciated that a function of VGAM1092 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1092 correlate with, and may be deduced from, the identity of the host target genes which VGAM1092 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[39723] Nucleotide sequences of the VGAM1092 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1092 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1092 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1092 are further described hereinbelow with reference to Table 1.

[39724] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1092 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1092 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39725] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1092 gene, herein designated VGAM is inhibition of expression of VGAM1092 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1092 correlate with, and may be deduced from, the identity of the target genes which VGAM1092 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[39726] GRB2-associated Binding Protein 3 (GAB3, Accession NM_080612) is a VGAM1092 host target gene. GAB3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GAB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB3 BINDING SITE, designated SEQ ID:27926, to the nucleotide sequence of VGAM1092 RNA, herein designated VGAM RNA, also designated SEQ ID:3803.

[39727] A function of VGAM1092 is therefore inhibition of GRB2-associated Binding Protein 3 (GAB3, Accession NM_080612). Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB3. LOC147093 (Accession XM_097184) is another VGAM1092 host target gene. LOC147093 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147093 BINDING SITE, desig-

nated SEQ ID:40802, to the nucleotide sequence of VGAM1092 RNA, herein designated VGAM RNA, also designated SEQ ID:3803.

[39728] Another function of VGAM1092 is therefore inhibition of LOC147093 (Accession XM_097184). Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147093. LOC169943 (Accession XM_104687) is another VGAM1092 host target gene. LOC169943 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169943 BINDING SITE, designated SEQ ID:42184, to the nucleotide sequence of VGAM1092 RNA, herein designated VGAM RNA, also designated SEQ ID:3803.

[39729] Another function of VGAM1092 is therefore inhibition of LOC169943 (Accession XM_104687). Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169943. LOC222128 (Accession XM_166560) is another VGAM1092 host target gene. LOC222128 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222128 BINDING SITE, designated SEQ ID:44538, to the nucleotide sequence of VGAM1092 RNA, herein designated VGAM RNA, also designated SEQ ID:3803.

[39730] Another function of VGAM1092 is therefore inhibition of LOC222128 (Accession XM_166560). Accordingly, utilities of VGAM1092 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222128. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1093 (VGAM1093) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39731] VGAM1093 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1093 was detected is described hereinabove with reference to Figs. 1-8.

[39732] VGAM1093 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Poinsettia Mosaic Virus. VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39733] VGAM1093 gene encodes a VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1093 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1093 precursor RNA is designated SEQ ID:1079, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1079 is located at position 3299 relative to the genome of Poinsettia Mosaic Virus.

[39734] VGAM1093 precursor RNA folds onto itself, forming VGAM1093 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[39735] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1093 folded precursor RNA into VGAM1093 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1093 RNA is designated SEQ ID:3804, and is provided hereinbelow with reference to the sequence listing part.

[39736] VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1093 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39737] VGAM1093 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1093 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1093 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1093 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39738] The complementary binding of VGAM1093 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1093 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1093 host target RNA into VGAM1093 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39739] It is appreciated that VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1093 host target genes. The mRNA of each one of this plurality of VGAM1093 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1093 RNA, herein designated VGAM RNA, and which when bound by VGAM1093 RNA causes inhibition of translation of respective one or more VGAM1093 host target proteins.

[39740] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1093 gene, herein designated VGAM GENE, on one or more VGAM1093 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39741] It is yet further appreciated that a function of VGAM1093 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1093 correlate with, and may be deduced from, the identity of the host target genes which VGAM1093 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39742] Nucleotide sequences of the VGAM1093 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1093 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1093 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1093 are further described hereinbelow with reference to Table 1.

[39743] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1093 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1093 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39744] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1093 gene, herein designated VGAM is inhibition of expression of VGAM1093 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1093 correlate with, and may be deduced from, the identity of the target genes which VGAM1093 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39745] AF9Q34 (Accession NM_032552) is a VGAM1093 host target gene. AF9Q34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AF9Q34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of AF9Q34 BINDING SITE, designated SEQ ID:26274, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39746] A function of VGAM1093 is therefore inhibition of AF9Q34 (Accession NM_032552). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF9Q34. Chromosome 20 Open Reading Frame 54 (C20orf54, Accession NM_033409) is another VGAM1093 host target gene. C20orf54 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf54, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf54 BINDING SITE, designated SEQ ID:27228, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39747] Another function of VGAM1093 is therefore inhibition of Chromosome 20 Open Reading Frame 54 (C20orf54, Accession NM_033409). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with C20orf54.

FLJ20034 (Accession NM_017630) is another VGAM1093 host target gene. FLJ20034 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20034 BINDING SITE, designated SEQ ID:19134, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39748] Another function of VGAM1093 is therefore inhibition of FLJ20034 (Accession NM_017630). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20034. KIAA0853 (Accession NM_015070) is another VGAM1093 host target gene. KIAA0853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0853 BINDING SITE, designated SEQ ID:17438, to the

nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39749] Another function of VGAM1093 is therefore inhibition of KIAA0853 (Accession NM_015070). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0853. MGC13071 (Accession NM_032689) is another VGAM1093 host target gene. MGC13071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13071 BINDING SITE, designated SEQ ID:26408, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39750] Another function of VGAM1093 is therefore inhibition of MGC13071 (Accession NM_032689). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13071. Neuronal Guanine Nucleotide Exchange Factor (NGEF, Accession XM_044799) is another VGAM1093 host target gene. NGEF BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by NGEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGEF BINDING SITE, designated SEQ ID:34278, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39751] Another function of VGAM1093 is therefore inhibition of Neuronal Guanine Nucleotide Exchange Factor (NGEF, Accession XM_044799). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGEF. Polymerase (RNA) II (DNA directed) Polypeptide D (POLR2D, Accession NM_004805) is another VGAM1093 host target gene. POLR2D BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POLR2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLR2D BINDING SITE, designated SEQ ID:11227, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ

ID:3804.

[39752] Another function of VGAM1093 is therefore inhibition of Polymerase (RNA) II (DNA directed) Polypeptide D (POLR2D, Accession NM_004805). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLR2D. Wiskott–Aldrich Syndrome–like (WASL, Accession NM_003941) is another VGAM1093 host target gene. WASL BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by WASL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WASL BINDING SITE, designated SEQ ID:10051, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39753] Another function of VGAM1093 is therefore inhibition of Wiskott–Aldrich Syndrome–like (WASL, Accession NM_003941). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WASL. LOC151512 (Accession XM_098072) is another VGAM1093 host target gene. LOC151512 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by LOC151512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151512 BINDING SITE, designated SEQ ID:41362, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39754] Another function of VGAM1093 is therefore inhibition of LOC151512 (Accession XM_098072). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151512. LOC153277 (Accession XM_098346) is another VGAM1093 host target gene. LOC153277 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153277 BINDING SITE, designated SEQ ID:41605, to the nucleotide sequence of VGAM1093 RNA, herein designated VGAM RNA, also designated SEQ ID:3804.

[39755] Another function of VGAM1093 is therefore inhibition of

LOC153277 (Accession XM_098346). Accordingly, utilities of VGAM1093 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153277. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1094 (VGAM1094) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39756] VGAM1094 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1094 was detected is described hereinabove with reference to Figs. 1-8.

[39757] VGAM1094 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Poinsettia Mosaic Virus. VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39758] VGAM1094 gene encodes a VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1094 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1094 precursor RNA is designated SEQ ID:1080, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1080 is located at position 5436 relative to the genome of Poinsettia Mosaic Virus.

[39759] VGAM1094 precursor RNA folds onto itself, forming VGAM1094 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[39760] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1094 folded precursor RNA into VGAM1094 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1094 RNA is designated SEQ ID:3805, and is provided hereinbelow with reference to the sequence listing part.

[39761] VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1094 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39762] VGAM1094 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1094 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1094 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1094 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39763] The complementary binding of VGAM1094 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1094 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1094 host target RNA into VGAM1094 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39764] It is appreciated that VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1094 host target genes. The mRNA of each one of this plurality of VGAM1094 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1094 RNA, herein designated VGAM RNA, and which when bound by VGAM1094 RNA causes inhibition of translation of respective one or more VGAM1094 host target proteins.

[39765] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1094 gene, herein designated VGAM GENE, on one or more VGAM1094 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39766] It is yet further appreciated that a function of VGAM1094 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1094 include diagnosis, prevention and treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1094 correlate with, and may be deduced from, the identity of the host target genes which VGAM1094 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39767] Nucleotide sequences of the VGAM1094 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1094 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1094 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1094 are further described hereinbelow with reference to Table 1.

[39768] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1094 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1094 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39769] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1094 gene, herein designated VGAM is inhibition of expression of VGAM1094 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1094 correlate with, and may be deduced from, the identity of the target genes which VGAM1094 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39770] LOC153937 (Accession XM_087813) is a VGAM1094 host target gene. LOC153937 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39443, to the nucleotide sequence of VGAM1094 RNA, herein designated VGAM RNA, also designated SEQ ID:3805.

[39771] A function of VGAM1094 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM1094 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153937. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1095 (VGAM1095) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39772] VGAM1095 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1095 was detected is described hereinabove with reference to Figs. 1–8.

[39773] VGAM1095 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Poinsettia Mosaic Virus. VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[39774] VGAM1095 gene encodes a VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1095 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1095 precursor RNA is designated SEQ ID:1081, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1081 is located at position 973 relative to the genome of Poinsettia Mosaic Virus.

[39775] VGAM1095 precursor RNA folds onto itself, forming VGAM1095 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39776] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1095 folded precursor RNA into VGAM1095 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1095 RNA is designated SEQ ID:3806, and is provided hereinbelow with reference to the sequence listing part.

[39777] VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1095 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39778] VGAM1095 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1095 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1095 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39779] The complementary binding of VGAM1095 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1095 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1095 host target RNA into VGAM1095 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39780] It is appreciated that VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1095 host target genes. The mRNA of each one of this plurality of VGAM1095 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1095 RNA, herein designated VGAM RNA, and which when bound by VGAM1095 RNA causes inhibition of translation of respective one or more VGAM1095 host target proteins.

[39781] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1095 gene, herein designated VGAM GENE, on one or more VGAM1095 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39782] It is yet further appreciated that a function of VGAM1095 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1095 correlate with, and may be deduced from, the identity of the host target genes which VGAM1095 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39783] Nucleotide sequences of the VGAM1095 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1095 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1095 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1095 are further described hereinbelow with reference to Table 1.

[39784] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1095 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1095 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39785] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1095 gene, herein designated VGAM is inhibition of expression of VGAM1095 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1095 correlate with, and may be deduced from, the identity of the target genes which VGAM1095 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39786] Amiloride-sensitive Cation Channel 1, Neuronal (degenerin) (ACCN1, Accession NM_001094) is a VGAM1095 host target gene. ACCN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACCN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACCN1 BINDING SITE, designated SEQ ID:6753, to the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA,

also designated SEQ ID:3806.

[39787] A function of VGAM1095 is therefore inhibition of Amiloride-sensitive Cation Channel 1, Neuronal (degenerin) (ACCN1, Accession NM_001094), a gene which non-voltage-gated amiloride-sensitive cation channel permeable for sodium, potassium and lithium. Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACCN1. The function of ACCN1 has been established by previous studies. Price et al. (1996) cloned a novel cDNA encoding a nonvoltage-dependent sodium channel from human brain, which they termed BNC1 for 'brain Na⁺ channel 1.' BNC1 has some sequence similarity to members of a family of amiloride-sensitive sodium channels that includes the mammalian epithelial Na⁺ channel (OMIM Ref. No. 600228). However, among other dissimilarities, BNC1 channel activity does not increase when it is coexpressed with other cloned subunits of the family. Thus, Price et al. (1996) considered BNC1 to be the first cloned member of a new subfamily of mammalian Na⁺ channels. Northern blot analysis revealed that the gene is expressed as 2.7- and 3.7-kb transcripts in brain and spinal cord tissues only. Price et al. (1996) sug-

gested that BNC1 may play a novel role in neurotransmission. Animal model experiments lend further support to the function of ACCN1. Price et al. (2000) generated mice deficient in Bnc1 by targeted disruption. Bnc1 $-/-$ mice had markedly reduced sensitivity of a specific component of mechanosensation: low-threshold rapidly adapting mechanoreceptors.

[39788] It is appreciated that the abovementioned animal model for ACCN1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[39789] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39790] Price, M. P.; Snyder, P. M.; Welsh, M. J. : Cloning and expression of a novel human brain Na⁺ channel. J. Biol. Chem. 271: 7879–7882, 1996. ; and

[39791] Price, M. P.; Lewin, G. R.; McIlwrath, S. L.; Cheng, C.; Xie, J.; Heppenstall, P. A.; Stucky, C. L.; Mannsfeldt, A. G.; Brennan, T. J.; Drummond, H. A.; Qiao, J.; Benson, C. J.; Tarr, D.

[39792] Further studies establishing the function and utilities of ACCN1 are found in John Hopkins OMIM database record

ID 601784, and in cited publications numbered 1251–1255 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM_004393) is another VGAM1095 host target gene. DAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE, designated SEQ ID:10636, to the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA, also designated SEQ ID:3806.

[39793] Another function of VGAM1095 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAG1. The function of DAG1 has been established by previous studies. Ibraghimov-Beskrovnaya et al. (1992) demonstrated that the trans-

membrane 43-kD and extracellular 156-kD dystrophin (OMIM Ref. No. 300377)–associated glycoproteins are encoded by a single messenger RNA and that the extracellular 156-kD DAG binds laminin. Thus, the 156-kD DAG is a laminin-binding glycoprotein that may provide linkage between the sarcolemma and extracellular matrix (ECM). The dramatic reduction in the 156K DAG in Duchenne muscular dystrophy (OMIM Ref. No. 310200) led to a loss of linkage between the sarcolemma and extracellular matrix, rendering muscle fibers more susceptible to necrosis. Ibraghimov-Beskrovnaya et al. (1992, 1992, 1993) mapped the DAG gene to chromosome 3 by Southern blot analysis of human/Chinese hamster somatic cell hybrid DNAs. One hybrid cell line with an isochromosome 3q was negative, suggesting location of the gene on 3p. The regional assignment was confirmed and further refined by fluorescence in situ hybridization, the localization being 3p21. The coding sequence of the DAG1 gene is organized into 2 exons, separated by a large intron (Ibraghimov-Beskrovnaya et al., 1993). The predicted amino acid sequence of human and rabbit dystroglycan are 93% identical, with predicted glycosylation sites being conserved. Human dystroglycan is expressed in a variety

of fetal and adult tissues. The muscle and nonmuscle isoforms of dystroglycan differ by carbohydrate moieties but not protein sequence. Using PCR, immunohistochemistry, and immunoblotting to analyze samples from patients with Fukuyama congenital muscular dystrophy (FCMD; 253800), Hayashi et al. (2001) confirmed a deficiency of fukutin and found marked deficiency of highly glycosylated DAG1 in skeletal and cardiac muscle and reduced amounts of DAG1 in brain tissue. Beta-dystroglycan was normal in all tissues examined. These findings supported the suggestion that fukutin deficiency affects the modification of glycosylation of DAG1, which then cannot localize or function properly and may be degraded or eluted from the extracellular surface membrane of the muscle fiber. Hayashi et al. (2001) concluded that this disruption underlies the developmental, structural, and functional damage to muscles in patients with FCMD. Animal model experiments lend further support to the function of DAG1. Cohn et al. (2002) found that striated muscle-specific disruption of the *Dag1* gene in mice resulted in loss of the dystrophin-glycoprotein complex in differentiated muscle and a remarkably mild muscular dystrophy with hypertrophy and without tissue fibrosis. They found that satellite

cells, expressing dystroglycan, supported continued efficient regeneration of skeletal muscle along with transient expression of dystroglycan in regenerating muscle fibers. Cohn et al. (2002) demonstrated a similar phenomenon of reexpression of functional dystroglycan in regenerating muscle fibers in a mild form of human muscular dystrophy caused by disruption of posttranslational dystroglycan processing. They concluded that maintenance of regenerative capacity by satellite cells expressing dystroglycan is likely responsible for mild disease progression in mice and possibly humans. Cohn et al. (2002) suggested that inadequate repair of skeletal muscle by satellite cells represents an important mechanism affecting the pathogenesis of muscular dystrophy.

[39794] It is appreciated that the abovementioned animal model for DAG1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[39795] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39796] Ibraghimov-Beskrovnaya, O.; Ervasti, J. M.; Leveille, C. J.; Slaughter, C. A.; Sernett, S. W.; Campbell, K. P. : Primary

structure of dystrophin-associated glycoproteins linking dystrophin to the extracellular matrix. Nature 355: 696–702, 1992. ; and

[39797] Hayashi, Y. K.; Ogawa, M.; Tagawa, K.; Noguchi, S.; Ishihara, T.; Nonaka, I.; Arahata, K. : Selective deficiency of alpha-dystroglycan in Fukuyama-type congenital muscular dystrophy. N.

[39798] Further studies establishing the function and utilities of DAG1 are found in John Hopkins OMIM database record ID 128239, and in cited publications numbered 4568–4570, 4604, 4615–4628, 4612–4613, 4608–461 and 4614 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM1095 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23714, to the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA, also designated SEQ ID:3806.

[39799] Another function of VGAM1095 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. SEPT6 (Accession NM_015129) is another VGAM1095 host target gene. SEPT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT6 BINDING SITE, designated SEQ ID:17494, to the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA, also designated SEQ ID:3806.

[39800] Another function of VGAM1095 is therefore inhibition of SEPT6 (Accession NM_015129). Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPT6. LOC91445 (Accession XM_018516) is another VGAM1095 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30371, to the nucleotide sequence of VGAM1095 RNA, herein designated VGAM RNA, also designated SEQ ID:3806.

[39801] Another function of VGAM1095 is therefore inhibition of LOC91445 (Accession XM_018516). Accordingly, utilities of VGAM1095 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91445. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1096 (VGAM1096) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39802] VGAM1096 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1096 was detected is described hereinabove with reference to Figs. 1-8.

[39803] VGAM1096 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mottle Virus.

VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39804] VGAM1096 gene encodes a VGAM1096 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1096 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1096 precursor RNA is designated SEQ ID:1082, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1082 is located at position 4444 relative to the genome of Strawberry Mottle Virus.

[39805] VGAM1096 precursor RNA folds onto itself, forming VGAM1096 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39806] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1096 folded precursor RNA into VGAM1096 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1096 RNA is designated SEQ ID:3807, and is provided hereinbelow with reference to the sequence listing part.

[39807] VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1096 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39808] VGAM1096 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1096 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1096 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39809] The complementary binding of VGAM1096 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1096 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1096 host target RNA into VGAM1096 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39810] It is appreciated that VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1096 host target genes. The mRNA of each one of this plurality of VGAM1096 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1096 RNA, herein designated VGAM RNA, and which when bound by VGAM1096 RNA causes inhibition of translation of respective one or more VGAM1096 host target proteins.

[39811] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1096 gene, herein designated VGAM GENE, on one or more VGAM1096 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39812] It is yet further appreciated that a function of VGAM1096 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1096 correlate with, and may be deduced from, the identity of the host target genes which VGAM1096 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39813] Nucleotide sequences of the VGAM1096 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1096 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1096 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1096 are further described hereinbelow with reference to Table 1.

[39814] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1096 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1096 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39815] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1096 gene, herein designated VGAM is inhibition of expression of VGAM1096 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1096 correlate with, and may be deduced from, the identity of the target genes which VGAM1096 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39816] ADP-ribosylation Factor 1 (ARF1, Accession XM_047545) is a VGAM1096 host target gene. ARF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF1 BINDING SITE, designated SEQ ID:34994, to the nucleotide se-

quence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39817] A function of VGAM1096 is therefore inhibition of ADP-ribosylation Factor 1 (ARF1, Accession XM_047545). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF1. Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM_001271) is another VGAM1096 host target gene. CHD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHD2 BINDING SITE, designated SEQ ID:6934, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39818] Another function of VGAM1096 is therefore inhibition of Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM_001271). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHD2. Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-

4 receptor) (ITGA4, Accession NM_000885) is another VGAM1096 host target gene. ITGA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA4 BINDING SITE, designated SEQ ID:6584, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39819] Another function of VGAM1096 is therefore inhibition of Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) (ITGA4, Accession NM_000885), a gene which recognizes one or more domains within the alternatively spliced cs-1 and cs-5 regions of fibronectin. Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA4. The function of ITGA4 has been established by previous studies. integrin family includes cell surface receptors for extracellular matrix components as well as receptors involved in various aspects of leukocyte adhesion. The integrins generally consist of alpha-beta heterodimeric transmembrane glycoproteins in which the al-

pha subunit is noncovalently associated with the beta subunit. Three major subfamilies of integrins have been defined, each containing a common beta subunit that can be associated with multiple alpha subunits. Two sets of integrins have been reported on lymphoid and myeloid cells. The first set, including LFA-1 (see OMIM Ref. No. 153370), Mac-1 (OMIM Ref. No. 120980), and p150,95 (OMIM Ref. No. 151510), represents the molecules that are exclusively expressed on leukocytes. The second set, the VLA antigens, are not restricted to leukocytes because nearly all of the cell types, except granulocytes and red blood cells, express them. They consist of at least 6 different chains that can associate with the same beta-1 subunit. These complexes are mainly involved in cell-matrix adhesive interactions. Within the VLA family, VLA4 is atypical because it participates not only in extracellular matrix adhesion as receptor for fibronectin but also as cell-cell adhesion receptor. Lu and Cyster (2002) studied the mechanisms that control localization of marginal zone B cells. They demonstrated that marginal zone B cells express elevated levels of the integrins LFA1 and alpha-4-beta-1 (see OMIM Ref. No. 135630), and that the marginal zone B cells bind to the ligands ICAM1 (OMIM

Ref. No. 147840) and VCAM1 (OMIM Ref. No. 192225).

These ligands are expressed within the marginal zone in a lymphotoxin-dependent manner. Combined inhibition of LFA1 and alpha-4-beta-1 causes a rapid and selective release of B cells from the marginal zone. Furthermore, lipopolysaccharide-triggered marginal zone B cell relocalization involves downregulation of integrin-mediated adhesion. Lu and Cyster (2002) concluded that their studies identified key requirements for marginal zone B cell localization and established a role for integrins in peripheral lymphoid tissue compartmentalization.

[39820] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39821] Lu, T. T.; Cyster, J. G. : Integrin-mediated long-term B cell retention in the splenic marginal zone. *Science* 297: 409-412, 2002. ; and

[39822] Cunningham, S. A.; Rodriguez, J. M.; Arrate, M. P.; Tran, T. M.; Brock, T. A. : JAM2 interacts with alpha-4/beta-1: facilitation by JAM3. *J. Biol. Chem.* 277: 27589-27592, 2002.

[39823] Further studies establishing the function and utilities of ITGA4 are found in John Hopkins OMIM database record

ID 192975, and in cited publications numbered 1001 and 10017–10018 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1319 (Accession NM_020770) is another VGAM1096 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1319 BINDING SITE, designated SEQ ID:21869, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39824] Another function of VGAM1096 is therefore inhibition of KIAA1319 (Accession NM_020770). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1319. KIAA1361 (Accession XM_030845) is another VGAM1096 host target gene. KIAA1361 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1361 BINDING SITE, designated SEQ ID:31171, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39825] Another function of VGAM1096 is therefore inhibition of KIAA1361 (Accession XM_030845). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1361. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM_031469) is another VGAM1096 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25533, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39826] Another function of VGAM1096 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM_031469). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with SH3BGRL2. LOC152008 (Accession XM_087363) is another VGAM1096 host target gene. LOC152008 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152008 BINDING SITE, designated SEQ ID:39197, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39827] Another function of VGAM1096 is therefore inhibition of LOC152008 (Accession XM_087363). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152008. LOC57826 (Accession NM_021183) is another VGAM1096 host target gene. LOC57826 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC57826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57826 BINDING SITE, designated SEQ ID:22159, to the

nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39828] Another function of VGAM1096 is therefore inhibition of LOC57826 (Accession NM_021183). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57826. LOC90333 (Accession XM_030958) is another VGAM1096 host target gene. LOC90333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90333 BINDING SITE, designated SEQ ID:31220, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39829] Another function of VGAM1096 is therefore inhibition of LOC90333 (Accession XM_030958). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90333. LOC90982 (Accession XM_035332) is another VGAM1096 host target gene. LOC90982 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC90982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90982 BINDING SITE, designated SEQ ID:32234, to the nucleotide sequence of VGAM1096 RNA, herein designated VGAM RNA, also designated SEQ ID:3807.

[39830] Another function of VGAM1096 is therefore inhibition of LOC90982 (Accession XM_035332). Accordingly, utilities of VGAM1096 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90982. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1097 (VGAM1097) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39831] VGAM1097 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1097 was detected is described hereinabove with reference to Figs. 1-8.

[39832] VGAM1097 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Strawberry Mottle Virus. VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39833] VGAM1097 gene encodes a VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1097 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1097 precursor RNA is designated SEQ ID:1083, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1083 is located at position 5799 relative to the genome of Strawberry Mottle Virus.

[39834] VGAM1097 precursor RNA folds onto itself, forming VGAM1097 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39835] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1097 folded precursor RNA into VGAM1097 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1097 RNA is designated SEQ ID:3808, and is provided hereinbelow with reference to the sequence listing part.

[39836] VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1097 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39837] VGAM1097 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1097 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1097 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39838] The complementary binding of VGAM1097 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1097 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1097

host target RNA into VGAM1097 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39839] It is appreciated that VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1097 host target genes. The mRNA of each one of this plurality of VGAM1097 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1097 RNA, herein designated VGAM RNA, and which when bound by VGAM1097 RNA causes inhibition of translation of respective one or more VGAM1097 host target proteins.

[39840] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1097 gene, herein designated VGAM GENE, on one or more VGAM1097 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39841] It is yet further appreciated that a function of VGAM1097 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1097 include diagnosis, prevention and treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1097 correlate with, and may be deduced from, the identity of the host target genes which VGAM1097 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39842] Nucleotide sequences of the VGAM1097 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1097 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1097 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1097 are further

described hereinbelow with reference to Table 1.

[39843] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1097 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1097 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39844] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1097 gene, herein designated VGAM is inhibition of expression of VGAM1097 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1097 correlate with, and may be deduced from, the identity of the target genes which VGAM1097 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39845] AAT1 (Accession XM_087415) is a VGAM1097 host target gene. AAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AAT1 BINDING SITE, designated SEQ ID:39228,

to the nucleotide sequence of VGAM1097 RNA, herein designated VGAM RNA, also designated SEQ ID:3808.

[39846] A function of VGAM1097 is therefore inhibition of AAT1 (Accession XM_087415), a gene which linkage between A1BG and Lutheran blood group . Accordingly, utilities of VGAM1097 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AAT1. The function of AAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM357.ACP33 (Accession NM_016630) is another VGAM1097 host target gene. ACP33 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ACP33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP33 BINDING SITE, designated SEQ ID:18745, to the nucleotide sequence of VGAM1097 RNA, herein designated VGAM RNA, also designated SEQ ID:3808.

[39847] Another function of VGAM1097 is therefore inhibition of ACP33 (Accession NM_016630). Accordingly, utilities of VGAM1097 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ACP33. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1098 (VGAM1098) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39848] VGAM1098 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1098 was detected is described hereinabove with reference to Figs. 1–8.

[39849] VGAM1098 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mottle Virus. VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39850] VGAM1098 gene encodes a VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1098 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1098 precursor RNA is designated SEQ ID:1084, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1084 is located at position 4573 relative to the genome of Strawberry Mottle Virus.

- [39851] VGAM1098 precursor RNA folds onto itself, forming VGAM1098 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39852] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1098 folded precursor RNA into VGAM1098 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1098 RNA is designated SEQ ID:3809, and is provided hereinbelow with reference to the sequence listing part.

[39853] VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1098 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39854] VGAM1098 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1098 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1098 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[39855] The complementary binding of VGAM1098 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1098 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1098 host target RNA into VGAM1098 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39856] It is appreciated that VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1098 host target genes. The mRNA of each one of this plurality of VGAM1098 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1098 RNA, herein designated VGAM RNA, and which when bound by VGAM1098 RNA causes

inhibition of translation of respective one or more VGAM1098 host target proteins.

[39857] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1098 gene, herein designated VGAM GENE, on one or more VGAM1098 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39858] It is yet further appreciated that a function of VGAM1098 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1098 include diagnosis, prevention and

treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1098 correlate with, and may be deduced from, the identity of the host target genes which VGAM1098 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39859] Nucleotide sequences of the VGAM1098 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1098 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1098 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1098 are further described hereinbelow with reference to Table 1.

[39860] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1098 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1098 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39861] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1098 gene, herein designated VGAM is inhibition of expression of VGAM1098 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1098 correlate with, and may be deduced from, the identity of the target genes which VGAM1098 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39862] Aryl-hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862) is a VGAM1098 host target gene. ARNT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNT2 BINDING SITE, designated SEQ ID:16938, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39863] A function of VGAM1098 is therefore inhibition of Aryl-hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862), a gene which specifically recognizes the xenobiotic response element (xre). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNT2. The function of ARNT2 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM_007163) is another VGAM1098 host target gene. SLC14A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC14A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC14A2 BINDING SITE, designated SEQ ID:14010, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39864] Another function of VGAM1098 is therefore inhibition of Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM_007163), a gene which is a renal urea transporter 2. Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC14A2. The function of SLC14A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Solute Carrier Family 6 (neurotransmitter trans-

porter, creatine), Member 8 (SLC6A8, Accession NM_005629) is another VGAM1098 host target gene. SLC6A8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC6A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A8 BINDING SITE, designated SEQ ID:12149, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39865] Another function of VGAM1098 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, creatine), Member 8 (SLC6A8, Accession NM_005629). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A8. T-cell Lymphoma Invasion and Metastasis 1 (TIAM1, Accession NM_003253) is another VGAM1098 host target gene. TIAM1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TIAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of TIAM1 BINDING SITE, designated SEQ ID:9260, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39866] Another function of VGAM1098 is therefore inhibition of T-cell Lymphoma Invasion and Metastasis 1 (TIAM1, Accession NM_003253), a gene which modulates the activity of Rho-like proteins and connects extracellular signals to cytoskeletal activities. Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAM1. The function of TIAM1 has been established by previous studies. To identify genes involved in metastasis by insertional mutagenesis, Habets et al. (1994) infected mouse BW5147 T-lymphoma cells with Moloney murine leukemia virus, resulting in 5 to 20 proviral insertions per cell. By this 'proviral tagging' method, invasive variants were selected on monolayers of fibroblasts. Disrupting proviral insertions were found in these cells within the coding exons of a gene designated Tiam1 (T-cell lymphoma invasion and metastasis-1). Selected clones were also metastatic in nude mice, and transfection of a truncated Tiam1 cDNA into noninvasive cells transmitted the invasive phenotype.

Northern blot analysis demonstrated highest expression in the brain and testis. The mouse cDNA was isolated from a brain library and shown to encode a 1,591-amino acid protein which is serine rich and has regions of similarity to the Dbl-homologous (DH) domain found in GDP-GTP exchangers. The protein sequence also contains a pleckstrin-homologous (PH) domain thought to be involved in protein-protein interactions. Habets et al. (1995) cloned the human TIAM1 cDNA from a brain library using the mouse cDNA as a probe. The human protein is 95% identical to the mouse homolog. The authors speculated that TIAM1 may function in cellular signaling by activation of a Rho-like GTPase that regulates the cytoskeletal organization. Animal model experiments lend further support to the function of TIAM1. Malliri et al. (2002) generated mice lacking Tiam1 and demonstrated that Tiam1 $-/-$ mice are resistant to the development of RAS-induced skin tumors initiated with 7,12-dimethylbenzanthracene and promoted with 12-O-tetradecanoylphorbol-13-acetate. Moreover, the few tumors produced in Tiam1 $-/-$ mice grew much slower than did tumors in wildtype mice. Tiam1-deficient primary embryonic fibroblasts were also resistant to

Ras(V12)–induced focus formation. Analysis of Tiam1 heterozygotes indicated that both tumor initiation and promotion were dependent on the TIAM1 gene dose. Tiam1 deficiency was associated with increased apoptosis during initiation and with impeded proliferation during promotion. Although the number of tumors in Tiam1 $-/-$ mice was small, a greater proportion progressed to malignancy, suggesting that Tiam1 deficiency promotes malignant conversion. Malliri et al. (2002) concluded that their studies identified RAC activator TIAM1 as a critical regulator of different aspects of Ras–induced tumor formation.

[39867] It is appreciated that the abovementioned animal model for TIAM1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[39868] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39869] Habets, G. G. M.; Scholtes, E. H. M.; Zuydgeest, D.; van der Kammen, R. A.; Stam, J. C.; Berns, A.; Collard, J. G. : Identification of an invasion–inducing gene, Tiam–1, that encodes a protein with homology to GDP–GTP exchangers for Rho–like proteins. Cell 77: 537–549, 1994. ; and

[39870] Malliri, A.; van der Kammen, R. A.; Clark, K.; van der Valk, M.; Michiels, F.; Collard, J. G. : Mice deficient in the Rac activator Tiam1 are resistant to Ras-induced skin tumours. *Natur.*

[39871] Further studies establishing the function and utilities of TIAM1 are found in John Hopkins OMIM database record ID 600687, and in cited publications numbered 9976–9980 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.ESDN (Accession NM_080927) is another VGAM1098 host target gene. ESDN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESDN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESDN BINDING SITE, designated SEQ ID:28155, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39872] Another function of VGAM1098 is therefore inhibition of ESDN (Accession NM_080927). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESDN. LIN-28 (Accession NM_024674) is another VGAM1098

host target gene. LIN-28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIN-28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIN-28 BINDING SITE, designated SEQ ID:23980, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39873] Another function of VGAM1098 is therefore inhibition of LIN-28 (Accession NM_024674). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIN-28. Syntrophin (SNPH, Accession NM_014723) is another VGAM1098 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16303, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39874] Another function of VGAM1098 is therefore inhibition of Syntaphilin (SNPH, Accession NM_014723). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. LOC146488 (Accession XM_047748) is another VGAM1098 host target gene. LOC146488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE, designated SEQ ID:35045, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39875] Another function of VGAM1098 is therefore inhibition of LOC146488 (Accession XM_047748). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC147229 (Accession XM_085742) is another VGAM1098 host target gene. LOC147229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147229, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147229 BINDING SITE, designated SEQ ID:38318, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39876] Another function of VGAM1098 is therefore inhibition of LOC147229 (Accession XM_085742). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147229. LOC200942 (Accession XM_114323) is another VGAM1098 host target gene. LOC200942 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200942, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200942 BINDING SITE, designated SEQ ID:42871, to the nucleotide sequence of VGAM1098 RNA, herein designated VGAM RNA, also designated SEQ ID:3809.

[39877] Another function of VGAM1098 is therefore inhibition of LOC200942 (Accession XM_114323). Accordingly, utilities of VGAM1098 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC200942. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1099 (VGAM1099) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39878] VGAM1099 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1099 was detected is described hereinabove with reference to Figs. 1–8.

[39879] VGAM1099 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African Swine Fever Virus. VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39880] VGAM1099 gene encodes a VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1099 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1099 precursor RNA is designated SEQ ID:1085, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1085 is located at position 122281 relative to the genome of African Swine Fever Virus.

- [39881] VGAM1099 precursor RNA folds onto itself, forming VGAM1099 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39882] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1099 folded precursor RNA into VGAM1099 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1099 RNA is designated SEQ ID:3810, and is provided hereinbelow with reference to the sequence listing part.

[39883] VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1099 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39884] VGAM1099 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1099 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1099 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[39885] The complementary binding of VGAM1099 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1099 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1099 host target RNA into VGAM1099 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39886] It is appreciated that VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1099 host target genes. The mRNA of each one of this plurality of VGAM1099 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1099 RNA, herein designated VGAM RNA, and which when bound by VGAM1099 RNA causes

inhibition of translation of respective one or more VGAM1099 host target proteins.

[39887] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1099 gene, herein designated VGAM GENE, on one or more VGAM1099 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39888] It is yet further appreciated that a function of VGAM1099 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1099 include diagnosis, prevention and

treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGAM1099 correlate with, and may be deduced from, the identity of the host target genes which VGAM1099 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39889] Nucleotide sequences of the VGAM1099 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1099 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1099 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1099 are further described hereinbelow with reference to Table 1.

[39890] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1099 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1099 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39891] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1099 gene, herein designated VGAM is inhibition of expression of VGAM1099 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1099 correlate with, and may be deduced from, the identity of the target genes which VGAM1099 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39892] Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147) is a VGAM1099 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42722, to the nucleotide sequence of VGAM1099 RNA, herein designated VGAM RNA, also designated SEQ ID:3810.

[39893] A function of VGAM1099 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1099 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM120.V-myb Myeloblastosis Viral Oncogene Homolog (avian) (MYB, Accession XM_004256) is another VGAM1099 host target gene. MYB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYB BINDING SITE, designated SEQ ID:29943, to the nucleotide sequence of VGAM1099 RNA, herein designated VGAM RNA, also designated SEQ ID:3810.

[39894] Another function of VGAM1099 is therefore inhibition of V-myb Myeloblastosis Viral Oncogene Homolog (avian) (MYB, Accession XM_004256). Accordingly, utilities of VGAM1099 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYB. MGC20253 (Accession NM_144583) is another VGAM1099 host target gene. MGC20253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MGC20253 BINDING SITE, designated SEQ ID:29395, to the nucleotide sequence of VGAM1099 RNA, herein designated VGAM RNA, also designated SEQ ID:3810.

[39895] Another function of VGAM1099 is therefore inhibition of MGC20253 (Accession NM_144583). Accordingly, utilities of VGAM1099 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20253. Serine/threonine Kinase 38 Like (STK38L, Accession XM_044823) is another VGAM1099 host target gene. STK38L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38L BINDING SITE, designated SEQ ID:34289, to the nucleotide sequence of VGAM1099 RNA, herein designated VGAM RNA, also designated SEQ ID:3810.

[39896] Another function of VGAM1099 is therefore inhibition of Serine/threonine Kinase 38 Like (STK38L, Accession XM_044823). Accordingly, utilities of VGAM1099 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with STK38L. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1100 (VGAM1100) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39897] VGAM1100 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1100 was detected is described hereinabove with reference to Figs. 1–8.

[39898] VGAM1100 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mottle Virus. VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39899] VGAM1100 gene encodes a VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1100 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1100 precursor RNA is designated SEQ ID:1086, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1086 is located at position 5104 relative to the genome of Strawberry Mottle Virus.

- [39900] VGAM1100 precursor RNA folds onto itself, forming VGAM1100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [39901] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1100 folded precursor RNA into VGAM1100 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1100 RNA is designated SEQ ID:3811, and is provided hereinbelow with reference to the sequence listing part.

[39902] VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1100 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39903] VGAM1100 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1100 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1100 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39904] The complementary binding of VGAM1100 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1100 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1100 host target RNA into VGAM1100 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39905] It is appreciated that VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1100 host target genes. The mRNA of each one of this plurality of VGAM1100 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1100 RNA, herein designated VGAM RNA, and which when bound by VGAM1100 RNA causes

inhibition of translation of respective one or more VGAM1100 host target proteins.

[39906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1100 gene, herein designated VGAM GENE, on one or more VGAM1100 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39907] It is yet further appreciated that a function of VGAM1100 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1100 include diagnosis, prevention and

treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1100 correlate with, and may be deduced from, the identity of the host target genes which VGAM1100 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39908] Nucleotide sequences of the VGAM1100 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1100 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1100 are further described hereinbelow with reference to Table 1.

[39909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1100 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1100 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39910] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1100 gene, herein designated VGAM is inhibition of expression of VGAM1100 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1100 correlate with, and may be deduced from, the identity of the target genes which VGAM1100 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39911] Engrailed Homolog 2 (EN2, Accession NM_001427) is a VGAM1100 host target gene. EN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN2 BINDING SITE, designated SEQ ID:7143, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39912] A function of VGAM1100 is therefore inhibition of Engrailed Homolog 2 (EN2, Accession NM_001427), a gene which may be required for normal cerebellar development; a homeobox protein, very strongly similar to murine En2. Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN2. The function of EN2 and its association with various diseases and clinical conditions, has

been established by previous studies, as described hereinabove with reference to VGAM232.SMG1 (Accession NM_015092) is another VGAM1100 host target gene. SMG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMG1 BINDING SITE, designated SEQ ID:17482, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39913] Another function of VGAM1100 is therefore inhibition of SMG1 (Accession NM_015092), a gene which acts as the target for the cell-cycle arrest and immunosuppressive effects. Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMG1. The function of SMG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419.FKSG42 (Accession NM_032032) is another VGAM1100 host target gene. FKSG42 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

FKSG42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKSG42 BINDING SITE, designated SEQ ID:25732, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39914] Another function of VGAM1100 is therefore inhibition of FKSG42 (Accession NM_032032). Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKSG42. KIAA0940 (Accession NM_014912) is another VGAM1100 host target gene. KIAA0940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0940 BINDING SITE, designated SEQ ID:17147, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39915] Another function of VGAM1100 is therefore inhibition of KIAA0940 (Accession NM_014912). Accordingly, utilities

of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0940. Polymerase (DNA directed), Mu (POLM, Accession XM_165867) is another VGAM1100 host target gene. POLM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLM BINDING SITE, designated SEQ ID:43784, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39916] Another function of VGAM1100 is therefore inhibition of Polymerase (DNA directed), Mu (POLM, Accession XM_165867). Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLM. Rac GTPase Activating Protein 1 (RACGAP1, Accession NM_013277) is another VGAM1100 host target gene. RACGAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RACGAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of RACGAP1 BINDING SITE, designated SEQ ID:14942, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39917] Another function of VGAM1100 is therefore inhibition of Rac GTPase Activating Protein 1 (RACGAP1, Accession NM_013277). Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RACGAP1. LOC201626 (Accession XM_114349) is another VGAM1100 host target gene. LOC201626 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201626, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201626 BINDING SITE, designated SEQ ID:42887, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39918] Another function of VGAM1100 is therefore inhibition of LOC201626 (Accession XM_114349). Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC201626. LOC91522 (Accession XM_038953) is another VGAM1100 host target gene. LOC91522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91522 BINDING SITE, designated SEQ ID:32962, to the nucleotide sequence of VGAM1100 RNA, herein designated VGAM RNA, also designated SEQ ID:3811.

[39919] Another function of VGAM1100 is therefore inhibition of LOC91522 (Accession XM_038953). Accordingly, utilities of VGAM1100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91522. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1101 (VGAM1101) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39920] VGAM1101 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1101 was detected is described hereinabove with reference to Figs. 1–8.

[39921] VGAM1101 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African Swine Fever Virus. VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39922] VGAM1101 gene encodes a VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1101 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1101 precursor RNA is designated SEQ ID:1087, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1087 is located at position 126143 relative to the genome of African Swine Fever Virus.

[39923] VGAM1101 precursor RNA folds onto itself, forming VGAM1101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39924] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1101 folded precursor RNA into VGAM1101 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1101 RNA is designated SEQ ID:3812, and is provided hereinbelow with reference to the sequence listing part.

[39925] VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1101 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39926] VGAM1101 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1101 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1101 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[39927] The complementary binding of VGAM1101 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1101 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1101 host target RNA into VGAM1101 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39928] It is appreciated that VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1101 host target genes. The mRNA of each one of this plurality of VGAM1101 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1101 RNA, herein designated VGAM RNA, and which when bound by VGAM1101 RNA causes inhibition of translation of respective one or more VGAM1101 host target proteins.

[39929] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1101 gene, herein designated VGAM GENE, on one or more VGAM1101 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39930] It is yet further appreciated that a function of VGAM1101 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGAM1101 correlate with, and may be deduced from, the identity of the host target genes which VGAM1101 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39931] Nucleotide sequences of the VGAM1101 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1101 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1101 are further described hereinbelow with reference to Table 1.

[39932] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1101 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1101 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39933] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1101 gene, herein designated VGAM is inhibition of expression of VGAM1101 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1101 correlate with, and may be deduced from, the identity of the target genes which VGAM1101 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39934] HRAS-like Suppressor (HRASLS, Accession NM_020386) is a VGAM1101 host target gene. HRASLS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HRASLS, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRASLS BINDING SITE, designated SEQ ID:21658, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39935] A function of VGAM1101 is therefore inhibition of HRAS-like Suppressor (HRASLS, Accession NM_020386), a gene which may regulate the Ha-ras-mediated signaling pathway. Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRASLS. The function of HRASLS has been established by previous studies. By differential display between 2 mouse cell lines, Akiyama et al. (1999) cloned a cDNA encoding a novel mouse protein, called A-C1, and showed that it modulates an HRAS (OMIM Ref. No. 190020)-mediated signaling pathway in vitro. Ito et al. (2001) isolated a partial cDNA encoding the human homolog, designated HRASLS, by RT-PCR with mRNA extracted from renal cell carcinoma cells. They used 5-prime and 3-prime RACE to obtain a full-length HRASLS cDNA encoding a 168-amino acid protein that shares 83% sequence identity with the mouse protein. HRASLS contains

2 consensus sequence motifs, DXXG and NKXD, suggesting involvement in a ras-signaling pathway. DXXG is involved in binding to Mg(2+) and gamma-phosphate when GTP is bound, and NKXD is important for binding to the guanine ring. Northern blot analysis detected expression of a 1.1-kb transcript in skeletal muscles, testis, heart, brain, and thyroid. Expression was also detected at low levels in normal bone, but at high levels in osteosarcoma cells.

[39936] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39937] Akiyama, H.; Hiraki, Y.; Noda, M.; Shigeno, C.; Ito, H.; Nakamura, T. : Molecular cloning and biological activity of a novel Ha-Ras suppressor gene predominantly expressed in skeletal muscle, heart, brain, and bone marrow by differential display using clonal mouse EC cells, ATDC5. J. Biol. Chem. 274: 32192-32197, 1999. ; and

[39938] Ito, H.; Akiyama, H.; Shigeno, C.; Nakamura, T. : Isolation, characterization, and chromosome mapping of a human A-C1 Ha-Ras suppressor gene (HRASLS). Cytogenet. Cell Genet. 93: 36-39.

[39939] Further studies establishing the function and utilities of

HRASLS are found in John Hopkins OMIM database record ID 606487, and in cited publications numbered 5552–5553 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 5 (SLC7A5, Accession NM_003486) is another VGAM1101 host target gene. SLC7A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A5 BINDING SITE, designated SEQ ID:9576, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39940] Another function of VGAM1101 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 5 (SLC7A5, Accession NM_003486), a gene which mediates transport of large and small neutral amino acids. Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A5. The function of SLC7A5 and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133333) is another VGAM1101 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE4, designated SEQ ID:28465, SEQ ID:28476, SEQ ID:17184 and SEQ ID:28448 respectively, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39941] Another function of VGAM1101 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133333), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM200. Chloride Intracellular Channel 5 (CLIC5, Accession NM_016929) is another VGAM1101 host target gene. CLIC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC5 BINDING SITE, designated SEQ ID:18845, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39942] Another function of VGAM1101 is therefore inhibition of Chloride Intracellular Channel 5 (CLIC5, Accession NM_016929). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC5. I(3)mbt-like (Drosophila) (L3MBTL, Accession XM_045421) is another VGAM1101 host target gene. L3MBTL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by L3MBTL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L3MBTL

BINDING SITE, designated SEQ ID:34457, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39943] Another function of VGAM1101 is therefore inhibition of I(3)mbt-like (Drosophila) (L3MBTL, Accession XM_045421). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L3MBTL. LOC149576 (Accession XM_086580) is another VGAM1101 host target gene. LOC149576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149576 BINDING SITE, designated SEQ ID:38776, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39944] Another function of VGAM1101 is therefore inhibition of LOC149576 (Accession XM_086580). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149576. LOC149668 (Accession XM_097692) is an-

other VGAM1101 host target gene. LOC149668 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149668 BINDING SITE, designated SEQ ID:41029, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39945] Another function of VGAM1101 is therefore inhibition of LOC149668 (Accession XM_097692). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149668. LOC221489 (Accession XM_168066) is another VGAM1101 host target gene. LOC221489 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221489 BINDING SITE, designated SEQ ID:44983, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39946] Another function of VGAM1101 is therefore inhibition of LOC221489 (Accession XM_168066). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221489. LOC84570 (Accession NM_032518) is another VGAM1101 host target gene. LOC84570 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC84570, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84570 BINDING SITE, designated SEQ ID:26266, to the nucleotide sequence of VGAM1101 RNA, herein designated VGAM RNA, also designated SEQ ID:3812.

[39947] Another function of VGAM1101 is therefore inhibition of LOC84570 (Accession NM_032518). Accordingly, utilities of VGAM1101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84570. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1102 (VGAM1102) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[39948] VGAM1102 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1102 was detected is described hereinabove with reference to Figs. 1–8.

[39949] VGAM1102 gene, herein designated VGAM GENE, is a viral gene contained in the genome of African Swine Fever Virus. VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39950] VGAM1102 gene encodes a VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1102 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1102 precursor RNA is designated SEQ ID:1088, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1088 is located at position 123478 relative to the genome of African Swine Fever Virus.

[39951] VGAM1102 precursor RNA folds onto itself, forming VGAM1102 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39952] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1102 folded precursor RNA into VGAM1102 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1102 RNA is designated SEQ ID:3813, and is provided hereinbelow with reference to the sequence listing part.

[39953] VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1102 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39954] VGAM1102 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1102 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1102 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39955] The complementary binding of VGAM1102 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1102 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1102 host target RNA into VGAM1102 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39956] It is appreciated that VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1102 host target genes. The mRNA of each one of this plurality of VGAM1102 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1102 RNA, herein designated VGAM RNA, and which when bound by VGAM1102 RNA causes inhibition of translation of respective one or more VGAM1102 host target proteins.

[39957] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1102 gene, herein designated VGAM GENE, on one or more VGAM1102 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[39958] It is yet further appreciated that a function of VGAM1102 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1102 include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGAM1102 correlate with, and may be deduced from, the identity of the host target genes which VGAM1102 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[39959] Nucleotide sequences of the VGAM1102 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1102 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1102 are further described hereinbelow with reference to Table 1.

[39960] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1102 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1102 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39961] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1102 gene, herein designated VGAM is inhibition of expression of VGAM1102 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1102 correlate with, and may be deduced from, the identity of the target genes which VGAM1102 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39962] Polypyrimidine Tract Binding Protein 2 (PTBP2, Accession NM_021190) is a VGAM1102 host target gene. PTBP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PTBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTBP2 BINDING SITE, designated SEQ ID:22168, to the nucleotide sequence of VGAM1102 RNA, herein designated VGAM RNA, also designated SEQ ID:3813.

[39963] A function of VGAM1102 is therefore inhibition of Polypyrimidine Tract Binding Protein 2 (PTBP2, Accession NM_021190). Accordingly, utilities of VGAM1102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTBP2. Zinc Finger Protein 36, C3H Type-like 2 (ZFP36L2, Accession NM_006887) is another VGAM1102 host target gene. ZFP36L2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZFP36L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP36L2 BINDING SITE, designated SEQ ID:13753, to the

nucleotide sequence of VGAM1102 RNA, herein designated VGAM RNA, also designated SEQ ID:3813.

[39964] Another function of VGAM1102 is therefore inhibition of Zinc Finger Protein 36, C3H Type-like 2 (ZFP36L2, Accession NM_006887). Accordingly, utilities of VGAM1102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP36L2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1103 (VGAM1103) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[39965] VGAM1103 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1103 was detected is described hereinabove with reference to Figs. 1–8.

[39966] VGAM1103 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mottle Virus. VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[39967] VGAM1103 gene encodes a VGAM1103 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1103 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1103 precursor RNA is designated SEQ ID:1089, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1089 is located at position 1299 relative to the genome of Strawberry Mottle Virus.

[39968] VGAM1103 precursor RNA folds onto itself, forming VGAM1103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[39969] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1103 folded precursor RNA into VGAM1103 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1103 RNA is designated SEQ ID:3814, and is provided hereinbelow with reference to the sequence listing part.

[39970] VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1103 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[39971] VGAM1103 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1103 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1103 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[39972] The complementary binding of VGAM1103 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1103 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1103 host target RNA into VGAM1103 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[39973] It is appreciated that VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1103 host target genes. The mRNA of each one of this plurality of VGAM1103 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1103 RNA, herein designated VGAM RNA, and which when bound by VGAM1103 RNA causes inhibition of translation of respective one or more VGAM1103 host target proteins.

[39974] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1103 gene, herein designated VGAM GENE, on one or more VGAM1103 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[39975] It is yet further appreciated that a function of VGAM1103 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1103 correlate with, and may be deduced from, the identity of the host target genes which VGAM1103 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[39976] Nucleotide sequences of the VGAM1103 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1103 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1103 are further described hereinbelow with reference to Table 1.

[39977] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1103 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1103 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[39978] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1103 gene, herein designated VGAM is inhibition of expression of VGAM1103 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1103 correlate with, and may be deduced from, the identity of the target genes which VGAM1103 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[39979] Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055) is a VGAM1103 host target gene. GFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFAP BINDING SITE, designated SEQ ID:7813, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39980] A function of VGAM1103 is therefore inhibition of Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055).

Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFAP. Huntingtin Interacting Protein 2 (HIP2, Accession NM_005339) is another VGAM1103 host target gene. HIP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIP2 BINDING SITE, designated SEQ ID:11814, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39981] Another function of VGAM1103 is therefore inhibition of Huntingtin Interacting Protein 2 (HIP2, Accession NM_005339). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIP2. Interleukin 15 Receptor, Alpha (IL15RA, Accession NM_002189) is another VGAM1103 host target gene. IL15RA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL15RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL15RA BINDING SITE, designated SEQ ID:7946, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39982] Another function of VGAM1103 is therefore inhibition of Interleukin 15 Receptor, Alpha (IL15RA, Accession NM_002189), a gene which is essential for signal transduction. Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL15RA. The function of IL15RA has been established by previous studies. Interleukin 2 (OMIM Ref. No. 147680) and interleukin 15 (OMIM Ref. No. 600554) are cytokines with overlapping but distinct biologic effects. Their receptors share 2 subunits, the IL2R beta (OMIM Ref. No. 146710) and gamma (OMIM Ref. No. 308380) chains, which are essential for signal transduction. The IL2 receptor requires an additional IL2-specific alpha subunit for high affinity IL2 binding (OMIM Ref. No. 147730). Giri et al. (1995) identified and cloned a murine IL15-specific alpha subunit and showed that it is structurally related to IL2R-alpha. However, the murine IL15R-alpha alone bound IL15 with a 1,000-fold higher

affinity than that seen with IL2R-alpha and IL2. Anderson et al. (1995) extended these studies into the human system with the isolation of 3 differentially spliced human IL15R-alpha variants that are all capable of high affinity binding of IL15. The cytoplasmic domain of IL15R-alpha, like that of IL2R-alpha is dispensable for mitogenic signaling, suggesting that the primary role of the alpha chains is to confer high affinity binding. At high concentrations, IL-15, like IL-2, is able to signal through a complex of IL2R-beta and -gamma in the absence of the alpha subunit. Furthermore, the IL15RA and IL2RA genes have a similar intron/exon organization and are closely linked in both human and murine genomes. The IL2RA gene (OMIM Ref. No. 147730) had been previously mapped to 10p15-p14 and its homolog to mouse chromosome 2. The human gene IL15RA was mapped to 10p15-p14 by fluorescence in situ hybridization and the mouse Il15ra gene was mapped to chromosome 2 by interspecific backcross mapping.

[39983] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[39984] Anderson, D. M.; Kumaki, S.; Ahdieh, M.; Bertles, J.;

Tometsko, M.; Loomis, A.; Giri, J.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Valentine, V.; Shapiro, D. N.; Morris, S. W.; Park, L. S.; Cosman, D. : Functional characterization of the human interleukin-15 receptor alpha chain and close linkage of IL15RA and IL2RA genes. J. Biol. Chem. 270: 29862-29869, 1995. ; and

[39985] Giri, J. G.; Kumaki, S.; Ahdieh, M.; Friend, D. J.; Loomis, A.; Shanebeck, K.; DuBose, R.; Cosman, D.; Park, L. S.; Anderson, D. M. : Identification and cloning of a novel IL-15 binding.

[39986] Further studies establishing the function and utilities of IL15RA are found in John Hopkins OMIM database record ID 601070, and in cited publications numbered 7860-7861 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LIM Domain Kinase 1 (LIMK1, Accession NM_016735) is another VGAM1103 host target gene. LIMK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE, designated SEQ ID:18795, to the nucleotide sequence of

VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39987] Another function of VGAM1103 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_016735). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Podocalyxin-like (PODXL, Accession NM_005397) is another VGAM1103 host target gene. PODXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PODXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PODXL BINDING SITE, designated SEQ ID:11871, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39988] Another function of VGAM1103 is therefore inhibition of Podocalyxin-like (PODXL, Accession NM_005397), a gene which is an antiadhesin. Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PODXL. The function of PODXL and its association with various

diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.COE2 (Accession XM_034639) is another VGAM1103 host target gene. COE2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COE2 BINDING SITE, designated SEQ ID:32126, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39989] Another function of VGAM1103 is therefore inhibition of COE2 (Accession XM_034639). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COE2. DKFZp547H236 (Accession XM_085929) is another VGAM1103 host target gene. DKFZp547H236 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp547H236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of DKFZp547H236 BINDING SITE, designated SEQ ID:38405, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39990] Another function of VGAM1103 is therefore inhibition of DKFZp547H236 (Accession XM_085929). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547H236. Epididymal Sperm Binding Protein 1 (ELSPBP1, Accession NM_022142) is another VGAM1103 host target gene. ELSPBP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ELSPBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELSPBP1 BINDING SITE, designated SEQ ID:22704, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39991] Another function of VGAM1103 is therefore inhibition of Epididymal Sperm Binding Protein 1 (ELSPBP1, Accession NM_022142). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with ELSPBP1. Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665) is another VGAM1103 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12210, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39992] Another function of VGAM1103 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. FLJ10853 (Accession NM_018246) is another VGAM1103 host target gene. FLJ10853 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated SEQ

ID:20214, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39993] Another function of VGAM1103 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. FLJ12770 (Accession NM_032174) is another VGAM1103 host target gene. FLJ12770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12770, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12770 BINDING SITE, designated SEQ ID:25885, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39994] Another function of VGAM1103 is therefore inhibition of FLJ12770 (Accession NM_032174). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12770. FLJ13491 (Accession NM_024623) is another VGAM1103 host target gene. FLJ13491 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13491, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13491 BINDING SITE, designated SEQ ID:23887, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39995] Another function of VGAM1103 is therefore inhibition of FLJ13491 (Accession NM_024623). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13491. FLJ14166 (Accession NM_024565) is another VGAM1103 host target gene. FLJ14166 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14166 BINDING SITE, designated SEQ ID:23791, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39996] Another function of VGAM1103 is therefore inhibition of

FLJ14166 (Accession NM_024565). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14166. FLJ14564 (Accession XM_084459) is another VGAM1103 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564 BINDING SITE, designated SEQ ID:37595, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39997] Another function of VGAM1103 is therefore inhibition of FLJ14564 (Accession XM_084459). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14564. FLJ20315 (Accession NM_017763) is another VGAM1103 host target gene. FLJ20315 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ20315 BINDING SITE, designated SEQ ID:19378, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39998] Another function of VGAM1103 is therefore inhibition of FLJ20315 (Accession NM_017763). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20315. HTCD37 (Accession XM_041884) is another VGAM1103 host target gene. HTCD37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTCD37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTCD37 BINDING SITE, designated SEQ ID:33617, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[39999] Another function of VGAM1103 is therefore inhibition of HTCD37 (Accession XM_041884). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTCD37. KIAA0040 (Accession NM_014656) is another

VGAM1103 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16096, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40000] Another function of VGAM1103 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. KIAA0682 (Accession NM_016196) is another VGAM1103 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:18289, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40001] Another function of VGAM1103 is therefore inhibition of KIAA0682 (Accession NM_016196). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA1297 (Accession XM_051005) is another VGAM1103 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35712, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40002] Another function of VGAM1103 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1854 (Accession XM_049884) is another VGAM1103 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35525, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40003] Another function of VGAM1103 is therefore inhibition of KIAA1854 (Accession XM_049884). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. My015 (Accession XM_039512) is another VGAM1103 host target gene. My015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by My015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of My015 BINDING SITE, designated SEQ ID:33105, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40004] Another function of VGAM1103 is therefore inhibition of My015 (Accession XM_039512). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with My015.

LOC122553 (Accession XM_058630) is another VGAM1103 host target gene. LOC122553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122553 BINDING SITE, designated SEQ ID:36689, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40005] Another function of VGAM1103 is therefore inhibition of LOC122553 (Accession XM_058630). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122553. LOC149146 (Accession XM_086441) is another VGAM1103 host target gene. LOC149146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149146 BINDING SITE, designated SEQ ID:38654, to the nucleotide sequence of VGAM1103 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3814.

[40006] Another function of VGAM1103 is therefore inhibition of LOC149146 (Accession XM_086441). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149146. LOC150279 (Accession XM_086820) is another VGAM1103 host target gene. LOC150279 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150279 BINDING SITE, designated SEQ ID:38899, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40007] Another function of VGAM1103 is therefore inhibition of LOC150279 (Accession XM_086820). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150279. LOC150951 (Accession XM_097975) is another VGAM1103 host target gene. LOC150951 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150951, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150951 BINDING SITE, designated SEQ ID:41278, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40008] Another function of VGAM1103 is therefore inhibition of LOC150951 (Accession XM_097975). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150951. LOC158549 (Accession XM_098963) is another VGAM1103 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42005, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40009] Another function of VGAM1103 is therefore inhibition of LOC158549 (Accession XM_098963). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158549. LOC255252 (Accession XM_170779) is another VGAM1103 host target gene. LOC255252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255252 BINDING SITE, designated SEQ ID:45545, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40010] Another function of VGAM1103 is therefore inhibition of LOC255252 (Accession XM_170779). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255252. LOC255452 (Accession XM_174088) is another VGAM1103 host target gene. LOC255452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255452 BINDING SITE, designated SEQ ID:46573, to

the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40011] Another function of VGAM1103 is therefore inhibition of LOC255452 (Accession XM_174088). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255452. LOC257428 (Accession XM_168584) is another VGAM1103 host target gene. LOC257428 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257428 BINDING SITE, designated SEQ ID:45260, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40012] Another function of VGAM1103 is therefore inhibition of LOC257428 (Accession XM_168584). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257428. LOC55831 (Accession NM_018447) is another VGAM1103 host target gene. LOC55831 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC55831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55831 BINDING SITE, designated SEQ ID:20516, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40013] Another function of VGAM1103 is therefore inhibition of LOC55831 (Accession NM_018447). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55831. LOC91050 (Accession XM_035703) is another VGAM1103 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32334, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40014] Another function of VGAM1103 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities

of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. LOC91149 (Accession XM_036480) is another VGAM1103 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32456, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40015] Another function of VGAM1103 is therefore inhibition of LOC91149 (Accession XM_036480). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91149. LOC91748 (Accession XM_040343) is another VGAM1103 host target gene. LOC91748 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC91748 BINDING SITE, designated SEQ ID:33286, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40016] Another function of VGAM1103 is therefore inhibition of LOC91748 (Accession XM_040343). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91748. LOC91759 (Accession XM_040467) is another VGAM1103 host target gene. LOC91759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91759 BINDING SITE, designated SEQ ID:33303, to the nucleotide sequence of VGAM1103 RNA, herein designated VGAM RNA, also designated SEQ ID:3814.

[40017] Another function of VGAM1103 is therefore inhibition of LOC91759 (Accession XM_040467). Accordingly, utilities of VGAM1103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91759. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1104 (VGAM1104) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40018] VGAM1104 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1104 was detected is described hereinabove with reference to Figs. 1–8.

[40019] VGAM1104 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 2. VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40020] VGAM1104 gene encodes a VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1104 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1104 precursor RNA is designated SEQ ID:1090, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1090 is located at position 94244 relative to the

genome of Human Herpesvirus 2.

[40021] VGAM1104 precursor RNA folds onto itself, forming VGAM1104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40022] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1104 folded precursor RNA into VGAM1104 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1104 RNA is designated SEQ ID:3815, and is provided hereinbelow with reference to the sequence listing part.

[40023] VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1104 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[40024] VGAM1104 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1104 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1104 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[40025] The complementary binding of VGAM1104 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1104 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1104 host target RNA into VGAM1104 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40026] It is appreciated that VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1104 host target genes. The mRNA of each one of this plurality of VGAM1104 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1104 RNA, herein designated VGAM RNA, and which when bound by VGAM1104 RNA causes inhibition of translation of respective one or more VGAM1104 host target proteins.

[40027] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1104 gene, herein designated VGAM GENE, on one or more VGAM1104 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40028] It is yet further appreciated that a function of VGAM1104 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1104 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1104

correlate with, and may be deduced from, the identity of the host target genes which VGAM1104 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40029] Nucleotide sequences of the VGAM1104 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1104 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1104 are further described hereinbelow with reference to Table 1.

[40030] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1104 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1104 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40031] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1104 gene, herein designated VGAM is inhibition of expression of VGAM1104 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1104 correlate with, and may be deduced

from, the identity of the target genes which VGAM1104 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40032] MGC15854 (Accession NM_145029) is a VGAM1104 host target gene. MGC15854 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15854 BINDING SITE, designated SEQ ID:29642, to the nucleotide sequence of VGAM1104 RNA, herein designated VGAM RNA, also designated SEQ ID:3815.

[40033] A function of VGAM1104 is therefore inhibition of MGC15854 (Accession NM_145029). Accordingly, utilities of VGAM1104 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15854. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1105 (VGAM1105) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[40034] VGAM1105 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1105 was detected is described hereinabove with reference to Figs. 1–8.

[40035] VGAM1105 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 2. VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40036] VGAM1105 gene encodes a VGAM1105 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1105 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1105 precursor RNA is designated SEQ ID:1091, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1091 is located at position 97913 relative to the genome of Human Herpesvirus 2.

[40037] VGAM1105 precursor RNA folds onto itself, forming VGAM1105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40038] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1105 folded precursor RNA into VGAM1105 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1105 RNA is designated SEQ ID:3816, and is provided hereinbelow with reference to the sequence listing part.

[40039] VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1105 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40040] VGAM1105 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1105 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1105 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[40041] The complementary binding of VGAM1105 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1105 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1105 host target RNA into VGAM1105 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40042] It is appreciated that VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1105 host target genes. The mRNA of each one of this plurality of VGAM1105 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1105 RNA, herein designated VGAM RNA, and which when bound by VGAM1105 RNA causes inhibition of translation of respective one or more VGAM1105 host target proteins.

[40043] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1105 gene, herein designated VGAM GENE, on one

or more VGAM1105 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40044] It is yet further appreciated that a function of VGAM1105 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1105 correlate with, and may be deduced from, the identity of the host target genes which VGAM1105 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40045] Nucleotide sequences of the VGAM1105 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1105 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1105 are further described hereinbelow with reference to Table 1.

[40046] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1105 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1105 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40047] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1105 gene, herein designated VGAM is inhibition of expression of VGAM1105 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1105 correlate with, and may be deduced from, the identity of the target genes which VGAM1105 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40048] Coatomer Protein Complex, Subunit Alpha (COPA, Acces-

sion NM_004371) is a VGAM1105 host target gene. COPA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by COPA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COPA BINDING SITE, designated SEQ ID:10591, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40049] A function of VGAM1105 is therefore inhibition of Coatomer Protein Complex, Subunit Alpha (COPA, Accession NM_004371), a gene which is involved protein transport between the endoplasmic reticulum (ER) and Golgi compartments. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COPA. The function of COPA has been established by previous studies. In eukaryotic cells, protein transport between the endoplasmic reticulum (ER) and Golgi compartments is mediated in part by non-clathrin-coated vesicular coat proteins (COPs). Seven COP subunits have been recognized, and represent components of a complex known as coatomer, or COPI. The subunits are designated alpha-COP, beta-COP (OMIM

Ref. No. 600959), beta-prime-COP, gamma-COP, delta-COP (OMIM Ref. No. 600820), epsilon-COP (OMIM Ref. No. 606942), and zeta-COP COPI is a heptameric protein recruited to membranes by ARF1 (OMIM Ref. No. 103180), a GTP-binding protein. Coat assembly helps in the transport of budding off membrane between the ER and Golgi apparatus. Using fluorescence microscopy, Presley et al. (2002) showed that guanine nucleotide exchange-activated ARF1 at the Golgi membrane recruits and binds cytoplasmic COPI to the membranes. Photobleaching experiments demonstrated that COPI remains at the membranes after ARF1 has been hydrolysed by GTPase-activating protein (GAP; 139150). COPI binds to membrane cargo, soluble-cargo receptors, or other Golgi proteins. Uncoating, or the release of COPI from Golgi membranes to the cytoplasm, then occurs, which is inhibited by AIF (PDIC8; 300169). Presley et al. (2002) concluded from their kinetic and biochemical analyses that COPI and ARF1 continuously bind and release from Golgi membranes, allowing the membrane at these sites to recruit cargo, alter their phospholipid composition, and become larger, phase-separated domains Chow (1997) reported the genomic organization of the COPA gene. It contains 33 exons ranging in size

from 67 to 611 bp. All exon–intron junctions conform with the GT–AG rule. The 32 introns range from about 80 bp to 4 kb, with the genomic DNA of COPA estimated to span approximately 37 kb. The untranscribed and non-coding portions of the 5–prime end of the gene lacked TATA and CAAT boxes but displayed a high GC content, consistent with its being a housekeeping gene

[40050] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40051] Presley, J. F.; Ward, T. H.; Pfeifer, A. C.; Siggia, E. D.; Phair, R. D.; Lippincott–Schwartz, J. : Dissection of COPI and Arf1 dynamics in vivo and role in Golgi membrane transport. *Nature* 417: 187–193, 2002. ; and

[40052] Quek, H. H.; Chow, V. T. K. : Genomic organization and mapping of the human HEP–COP gene (COPA) to 1q. *Cytogenet. Cell Genet.* 76: 139–143, 1997.

[40053] Further studies establishing the function and utilities of COPA are found in John Hopkins OMIM database record ID 601924, and in cited publications numbered 581 and 5812–5813 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Forkhead Box D1 (FOXD1, Accession NM_004472) is another

VGAM1105 host target gene. FOXD1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FOXD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXD1 BINDING SITE, designated SEQ ID:10779, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40054] Another function of VGAM1105 is therefore inhibition of Forkhead Box D1 (FOXD1, Accession NM_004472), a gene which has regulatory role in embryonic development. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXD1. The function of FOXD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM615. Glycogenin (GYG, Accession NM_004130) is another VGAM1105 host target gene. GYG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GYG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of GYG BINDING SITE, designated SEQ ID:10340, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40055] Another function of VGAM1105 is therefore inhibition of Glycogenin (GYG, Accession NM_004130), a gene which primes de novo glycogen synthesis. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GYG. The function of GYG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM777. Protein Tyrosine Phosphatase, Receptor Type, F (PTPRF, Accession NM_002840) is another VGAM1105 host target gene. PTPRF BINDING SITE1 and PTPRF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRF, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRF BINDING SITE1 and PTPRF BINDING SITE2, designated SEQ ID:8724 and SEQ ID:28198 respectively, to the nucleotide sequence of VGAM1105 RNA,

herein designated VGAM RNA, also designated SEQ ID:3816.

[40056] Another function of VGAM1105 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F (PTPRF, Accession NM_002840), a gene which negatively regulates the insulin signaling pathway. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRF. The function of PTPRF has been established by previous studies. The LAR gene (symbolized PTPRF) encodes a membrane protein that has a cytoplasmic domain with homology to protein-tyrosine phosphatase 1B (OMIM Ref. No. 176885) and an extracellular domain homologous to the neural cellular adhesion molecule NCAM (OMIM Ref. No. 116930). The human LAR molecule closely resembles cell adhesion molecules, which suggests that it may be involved in the regulation of phosphotyrosine levels through cell-cell or cell-matrix interactions. As a first step toward site-directed mutagenesis studies of LAR function, Schaapveld et al. (1995) characterized the mouse Ptp^rf gene. They found that its cytoplasmic region is encoded by 11 exons that span only 4.5 kb of genomic DNA. Compared to the known exon-intron structures of other mam-

malian receptor-like protein tyrosine phosphatase genes such as Ptp^{ra} (encoding LRP; 176884) and Ptp^{rc} (coding for Ly-5; 151460), the portion of the Ptp^{rf} gene encoding the cytoplasmic region of murine LAR contained not only smaller, but also fewer introns. O'Grady et al. (1994) demonstrated that the human LAR gene is composed of 33 exons spanning over 85 kb. Exon 2 encodes the signal sequence and the first 4 amino acids in the mature LAR protein. The 3 immunoglobulin-like domains are encoded by exons 3 to 7, and the 8 fibronectin type III (OMIM Ref. No. FN-III) domains by exons 8 to 17. Exons 18 to 22 encode the juxtamembrane and transmembrane domains, and exons 23 to 33 encode the 2 conserved tyrosine phosphatase domains and the entire 3-prime untranslated region. Alternative splicing of LAR mRNA was revealed by RT-PCR analysis.

[40057] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40058] Schaapveld, R. Q. J.; van den Maagdenberg, A. M. J. M.; Schepens, J. T. G.; Olde Weghuis, D.; Geurts van Kessel, A.; Wieringa, B.; Hendriks, W. J. A. J. : The mouse gene Ptp^{rf} encoding the leukocyte common antigen-related

molecule LAR: cloning, characterization, and chromosomal localization. Genomics 27: 124–130, 1995. ; and

[40059] O'Grady, P.; Krueger, N. X.; Streuli, M.; Saito, H. : Genomic organization of the human LAR protein tyrosine phosphatase gene and alternative splicing in the extracellular fibronectin ty.

[40060] Further studies establishing the function and utilities of PTPRF are found in John Hopkins OMIM database record ID 179590, and in cited publications numbered 12382–12390 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serum/glucocorticoid Regulated Kinase (SGK, Accession NM_005627) is another VGAM1105 host target gene. SGK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGK BINDING SITE, designated SEQ ID:12138, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40061] Another function of VGAM1105 is therefore inhibition of Serum/glucocorticoid Regulated Kinase (SGK, Accession

NM_005627), a gene which Serine/threonine kinase. Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGK. The function of SGK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM543.ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM1105 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31081, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40062] Another function of VGAM1105 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. Chromosome 20 Open Reading Frame 59 (C20orf59, Accession NM_022082) is

another VGAM1105 host target gene. C20orf59 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf59 BINDING SITE, designated SEQ ID:22623, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40063] Another function of VGAM1105 is therefore inhibition of Chromosome 20 Open Reading Frame 59 (C20orf59, Accession NM_022082). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf59.

FLJ31300 (Accession NM_144639) is another VGAM1105 host target gene. FLJ31300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31300 BINDING SITE, designated SEQ ID:29463, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3816.

[40064] Another function of VGAM1105 is therefore inhibition of FLJ31300 (Accession NM_144639). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31300. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM1105 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:28920 and SEQ ID:17399 respectively, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40065] Another function of VGAM1105 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with GGA2. KIAA1061 (Accession XM_048786) is another VGAM1105 host target gene. KIAA1061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1061 BINDING SITE, designated SEQ ID:35266, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40066] Another function of VGAM1105 is therefore inhibition of KIAA1061 (Accession XM_048786). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1061. MGC16386 (Accession NM_080668) is another VGAM1105 host target gene. MGC16386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16386 BINDING SITE, designated SEQ ID:27960, to the nucleotide sequence of VGAM1105 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3816.

[40067] Another function of VGAM1105 is therefore inhibition of MGC16386 (Accession NM_080668). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16386. MGC2835 (Accession NM_024072) is another VGAM1105 host target gene. MGC2835 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2835, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2835 BINDING SITE, designated SEQ ID:23501, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40068] Another function of VGAM1105 is therefore inhibition of MGC2835 (Accession NM_024072). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2835. Paralemmin (PALM, Accession NM_002579) is another VGAM1105 host target gene. PALM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PALM, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PALM BINDING SITE, designated SEQ ID:8436, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40069] Another function of VGAM1105 is therefore inhibition of Paralemmin (PALM, Accession NM_002579). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PALM. VMP1 (Accession NM_030938) is another VGAM1105 host target gene. VMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VMP1 BINDING SITE, designated SEQ ID:25206, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40070] Another function of VGAM1105 is therefore inhibition of VMP1 (Accession NM_030938). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with VMP1. LOC147299 (Accession XM_085763) is another VGAM1105 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38333, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40071] Another function of VGAM1105 is therefore inhibition of LOC147299 (Accession XM_085763). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. LOC147429 (Accession XM_085793) is another VGAM1105 host target gene. LOC147429 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147429 BINDING SITE, designated SEQ ID:38339, to

the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40072] Another function of VGAM1105 is therefore inhibition of LOC147429 (Accession XM_085793). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147429. LOC151512 (Accession XM_098072) is another VGAM1105 host target gene. LOC151512 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151512 BINDING SITE, designated SEQ ID:41364, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40073] Another function of VGAM1105 is therefore inhibition of LOC151512 (Accession XM_098072). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151512. LOC151525 (Accession XM_087231) is another VGAM1105 host target gene. LOC151525 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC151525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151525 BINDING SITE, designated SEQ ID:39131, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40074] Another function of VGAM1105 is therefore inhibition of LOC151525 (Accession XM_087231). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151525. LOC158055 (Accession XM_088453) is another VGAM1105 host target gene. LOC158055 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158055 BINDING SITE, designated SEQ ID:39703, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40075] Another function of VGAM1105 is therefore inhibition of LOC158055 (Accession XM_088453). Accordingly, utilities

of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158055. LOC255104 (Accession XM_170911) is another VGAM1105 host target gene. LOC255104 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255104 BINDING SITE, designated SEQ ID:45683, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40076] Another function of VGAM1105 is therefore inhibition of LOC255104 (Accession XM_170911). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255104. LOC256364 (Accession XM_170672) is another VGAM1105 host target gene. LOC256364 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256364 BINDING SITE, designated SEQ ID:45445, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40077] Another function of VGAM1105 is therefore inhibition of LOC256364 (Accession XM_170672). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256364. LOC51236 (Accession NM_016458) is another VGAM1105 host target gene. LOC51236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51236 BINDING SITE, designated SEQ ID:18573, to the nucleotide sequence of VGAM1105 RNA, herein designated VGAM RNA, also designated SEQ ID:3816.

[40078] Another function of VGAM1105 is therefore inhibition of LOC51236 (Accession NM_016458). Accordingly, utilities of VGAM1105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51236. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1106 (VGAM1106) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40079] VGAM1106 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1106 was detected is described hereinabove with reference to Figs. 1–8.

[40080] VGAM1106 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 2. VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40081] VGAM1106 gene encodes a VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1106 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1106 precursor RNA is designated SEQ ID:1092, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1092 is located at position 97030 relative to the

genome of Human Herpesvirus 2.

[40082] VGAM1106 precursor RNA folds onto itself, forming VGAM1106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40083] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1106 folded precursor RNA into VGAM1106 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1106 RNA is designated SEQ ID:3817, and is provided hereinbelow with reference to the sequence listing part.

[40084] VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1106 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40085] VGAM1106 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1106 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1106 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[40086] The complementary binding of VGAM1106 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1106 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1106 host target RNA into VGAM1106 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40087] It is appreciated that VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1106 host target genes. The mRNA of each one of this plurality of VGAM1106 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1106 RNA, herein designated VGAM RNA, and which when bound by VGAM1106 RNA causes inhibition of translation of respective one or more VGAM1106 host target proteins.

[40088] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1106 gene, herein designated VGAM GENE, on one or more VGAM1106 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40089] It is yet further appreciated that a function of VGAM1106 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1106 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1106

correlate with, and may be deduced from, the identity of the host target genes which VGAM1106 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40090] Nucleotide sequences of the VGAM1106 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1106 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1106 are further described hereinbelow with reference to Table 1.

[40091] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1106 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1106 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40092] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1106 gene, herein designated VGAM is inhibition of expression of VGAM1106 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1106 correlate with, and may be deduced

from, the identity of the target genes which VGAM1106 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40093] Paralemmin (PALM, Accession NM_002579) is a VGAM1106 host target gene. PALM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PALM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PALM BINDING SITE, designated SEQ ID:8437, to the nucleotide sequence of VGAM1106 RNA, herein designated VGAM RNA, also designated SEQ ID:3817.

[40094] A function of VGAM1106 is therefore inhibition of Paralemmin (PALM, Accession NM_002579). Accordingly, utilities of VGAM1106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PALM. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1107 (VGAM1107) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[40095] VGAM1107 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1107 was detected is described hereinabove with reference to Figs. 1–8.

[40096] VGAM1107 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Adenovirus C. VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40097] VGAM1107 gene encodes a VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1107 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1107 precursor RNA is designated SEQ ID:1093, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1093 is located at position 3553 relative to the genome of Porcine Adenovirus C.

[40098] VGAM1107 precursor RNA folds onto itself, forming VGAM1107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40099] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1107 folded precursor RNA into VGAM1107 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1107 RNA is designated SEQ ID:3818, and is provided hereinbelow with reference to the sequence listing part.

[40100] VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1107 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40101] VGAM1107 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1107 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1107 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[40102] The complementary binding of VGAM1107 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1107 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1107 host target RNA into VGAM1107 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40103] It is appreciated that VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1107 host target genes. The mRNA of each one of this plurality of VGAM1107 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1107 RNA, herein designated VGAM RNA, and which when bound by VGAM1107 RNA causes inhibition of translation of respective one or more VGAM1107 host target proteins.

[40104] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1107 gene, herein designated VGAM GENE, on one

or more VGAM1107 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40105] It is yet further appreciated that a function of VGAM1107 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of viral infection by Porcine Adenovirus C. Specific functions, and accordingly utilities, of VGAM1107 correlate with, and may be deduced from, the identity of the host target genes which VGAM1107 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40106] Nucleotide sequences of the VGAM1107 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1107 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1107 are further described hereinbelow with reference to Table 1.

[40107] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1107 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1107 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40108] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1107 gene, herein designated VGAM is inhibition of expression of VGAM1107 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1107 correlate with, and may be deduced from, the identity of the target genes which VGAM1107 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40109] APM1 (Accession NM_004797) is a VGAM1107 host target

gene. APM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APM1 BINDING SITE, designated SEQ ID:11207, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40110] A function of VGAM1107 is therefore inhibition of APM1 (Accession NM_004797). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APM1. BAI1-associated Protein 3 (BAIAP3, Accession NM_003933) is another VGAM1107 host target gene. BAIAP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAIAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAIAP3 BINDING SITE, designated SEQ ID:10036, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40111] Another function of VGAM1107 is therefore inhibition of BAI1-associated Protein 3 (BAIAP3, Accession NM_003933). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAIAP3. CD1D Antigen, D Polypeptide (CD1D, Accession XM_086610) is another VGAM1107 host target gene. CD1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD1D BINDING SITE, designated SEQ ID:38790, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40112] Another function of VGAM1107 is therefore inhibition of CD1D Antigen, D Polypeptide (CD1D, Accession XM_086610), a gene which is a member D of the CD1 family; involved in antigen presentation . Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD1D. The function of CD1D has been established by previous studies. Alpha-galactosylceramide

(alpha-GalCer), a marine sponge glycosphingolipid (GSL), and some disaccharide GSLs can be presented by CD1D in vitro without antigen-presenting cells (APCs) to NK T cells, which respond by producing interleukin-2 (IL2; 147680). Prigozy et al. (2001), however, found that sugars linked at the 2-prime or 3-prime position of the galactose must be removed by APCs in order to stimulate NK T cells. Immunofluorescence microscopy, supported by functional assays, showed that intact CD1D, but not cytoplasmic tail-deleted mutants lacking the endosomal-targeting motif, localized to lysosomes as well as to the plasma membrane, and could present 2-prime-linked alpha-GalGalCer to NK T cells. Such 2-prime-linked alpha-GalGalCer antigen presentation could be blocked by lysosomotropic inhibitors and specifically by an inhibitor of alpha-galactosidase A (GLA; 301500). Alternatively, alpha-galactosidase A-mediated removal of the terminal galactose permitted the presentation of the 2-prime-linked alpha-GalGalCer to NK T cells in the absence APCs. Prigozy et al. (2001) also found that splenic APCs from alpha-galactosidase A-deficient mice, a model of Fabry disease (OMIM Ref. No. 301500), could present alpha-GalCer or 6-prime-linked alpha-GalGalCer but not 2-prime-linked

alpha-GalGalCer to NK T-cell lines. Prigozy et al. (2001) concluded that the demonstration of a carbohydrate antigen-processing pathway could extend the range of antigens that are presented by CD1 molecules. Animal model experiments lend further support to the function of CD1D. Quantitative and qualitative defects in CD1-restricted natural killer T cells are found in autoimmune-prone strains of mice, including the nonobese diabetic (NOD) mouse. These defects appear to be associated with the emergence of spontaneous autoimmunity. Shi et al. (2001) demonstrated that CD1d-null NOD transgenic mice have accelerated onset and increased incidence of diabetes when compared with CD1d +/- and CD1d +/+ littermates. The pancreata of CD1d-null mice harbored significantly higher numbers of activated memory T cells expressing the chemokine receptor CCR4 (OMIM Ref. No. 604836). Notably, the presence of these T cells was associated with immunohistochemical evidence of increased destructive insulitis. Thus, CD1d-restricted T cells are critically important for regulation of the spontaneous disease process in NOD mice.

[40113] It is appreciated that the abovementioned animal model for CD1D is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[40114] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40115] Riese, R. J.; Shi, G.-P.; Villadangos, J.; Stetson, D.; Driessen, C.; Lennon-Dumenil, A.-M.; Chu, C.-L.; Naumov, Y.; Behar, S. M.; Ploegh, H.; Locksley, R.; Chapman, H. A. : Regulation of CD1 function and NK1.1+ T cell selection and maturation by cathepsin S. *Immunity* 15: 909-919, 2001. ; and

[40116] Prigozy, T. I.; Naidenko, O.; Qasba, P.; Elewaut, D.; Brossay, L.; Khurana, A.; Natori, T.; Koezuka, Y.; Kulkarni, A.; Kronenberg, M. : Glycolipid antigen processing for presentation b.

[40117] Further studies establishing the function and utilities of CD1D are found in John Hopkins OMIM database record ID 188410, and in cited publications numbered 9779-9781, 4748, 9782, 9783, 10279-9785, 219 and 9786 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDP-diacylglycerol Synthase (phosphatidate cytidylyltransferase) 2 (CDS2, Accession NM_003818) is another VGAM1107 host target gene.

CDS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDS2 BINDING SITE, designated SEQ ID:9910, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40118] Another function of VGAM1107 is therefore inhibition of CDP-diacylglycerol Synthase (phosphatidate cytidylyltransferase) 2 (CDS2, Accession NM_003818), a gene which is a key regulator of the amount of PIP2 available for signaling. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDS2. The function of CDS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM900. Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717) is another VGAM1107 host target gene. DGKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKI, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKI BINDING SITE, designated SEQ ID:11081, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40119] Another function of VGAM1107 is therefore inhibition of Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717), a gene which regulates the intracellular concentration of the second messenger diacylglycerol (DAG). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKI. The function of DGKI has been established by previous studies. Diacylglycerol kinase (DGK) plays a key role in cellular processes by regulating the intracellular concentration of the second messenger diacylglycerol (DAG). For background information on the DGKs, see 125855. Type IV DGKs, such as DGK-zeta (OMIM Ref. No. 601441), contain 4 C-terminal ankyrin repeats and a MARCKS (OMIM Ref. No. 177061) homology domain. Mutations in the *Drosophila* *rdgA* (retinal degeneration A) gene, a type IV DGK also referred to as DGK2, lead to degeneration of photoreceptor cells and blindness (Masai et al., 1993). By searching an EST database for sequences re-

lated to DGK-zeta, Ding et al. (1998) identified a cDNA encoding a novel DGK that they designated DGK-iota. The predicted 1,065-amino acid DGK-iota protein is a type IV DGK that shares 63% and 40% amino acid identity with DGK-zeta and rdgA, respectively. When expressed in mammalian cells, the DGK-iota protein had an apparent molecular weight of 130 kD and exhibited DGK activity. DGK-iota was found in both the nucleus and the cytoplasm, but expression of protein kinase C-alpha (OMIM Ref. No. 176960) or -gamma (OMIM Ref. No. 176980) attenuated the nuclear localization. Ding et al. (1998) concluded that the nuclear localization of DGK-iota is regulated by phosphorylation in much the same manner as that of DGK-zeta. Northern blot and RT-PCR analyses revealed that the DGK-iota gene was expressed specifically in brain and retina as a predominant transcript of more than 12 kb, including a very long 3-prime untranslated region. Additional low abundance transcripts of 9.5 and 7.5 kb were also detected. By FISH, Ding et al. (1998) mapped the DGK-iota gene to 7q32.3-q33. They suggested that DGK-iota is a candidate gene for a dominant form of retinitis pigmentosa (RP10; 180105) that maps to a locus in the same region.

[40120] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40121] Ding, L.; Traer, E.; McIntyre, T. M.; Zimmerman, G. A.; Prescott, S. M. : The cloning and characterization of a novel human diacylglycerol kinase, DGK- ι . J. Biol. Chem. 273: 32746–32752, 1998. ; and

[40122] Masai, I.; Okazaki, A.; Hosoya, T.; Hotta, Y. : Drosophila retinal degeneration A gene encodes an eye-specific diacylglycerol kinase with cysteine-rich zinc-finger motifs and ankyrin re.

[40123] Further studies establishing the function and utilities of DGKI are found in John Hopkins OMIM database record ID 604072, and in cited publications numbered 63 and 1267 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is another VGAM1107 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of FLRT2 BINDING SITE, designated SEQ ID:14878, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40124] Another function of VGAM1107 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Forkhead Box I1 (FOXI1, Accession NM_012188) is another VGAM1107 host target gene. FOXI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXI1 BINDING SITE, designated SEQ ID:14475, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3818.

[40125] Another function of VGAM1107 is therefore inhibition of Forkhead Box I1 (FOXI1, Accession NM_012188), a gene which plays an important role in the development of the cochlea and vestibulum, as well as embryogenesis. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXI1. The function of FOXI1 has been established by previous studies. FKH10 is a member of the forkhead family of winged helix transcription regulators. The forkhead family is distinguished by a characteristic 100-amino acid motif that was originally identified in *Drosophila* (see OMIM Ref. No. 164874). Pierrou et al. (1994) identified 7 human genes containing a forkhead domain and designated them forkhead related activators (FREAC) 1 through 7. Northern blot analysis revealed that the FREAC6, or FKHL10, gene is expressed as a 2.3-kb mRNA only in kidney. Genes encoding forkhead proteins are instrumental during embryogenesis in mammals, in particular during development of the nervous system. Hu-lander et al. (1998) reported that mice with a targeted disruption of the *Fkh10* locus exhibit circling behavior, poor swimming ability, and abnormal reaching response,

all common findings in mice with vestibular dysfunction. These animals also failed to elicit a Preyer reflex in response to a suprathreshold auditory stimulation, as seen in mice with profound hearing impairment. Histologic examination of the inner ear revealed a gross structural malformation of the vestibulum as well as of the cochlea. These structures were replaced by a single irregular cavity in which neither proper semicircular ducts nor cochlea could be identified. Hulander et al. (1998) also showed that at 9.5 days postcoitum (DPC), Fkh10 was exclusively expressed in the otic vesicle. Larsson et al. (1995) showed that FKHL10 is expressed in the adult and fetal kidney, whereas 15 other tissues (which did not include any inner ear-derived samples) were negative. Kidney-specific expression had been observed also in the mouse. Although Fkh10 may play a role in the kidney during later stages of development, it may be a minor, or perhaps redundant, role, as no kidney dysfunction was observed in homozygous knockout mice. On the contrary, Fkh10 appears to be unique in the sense that it is an early otic vesicle-specific gene necessary for the development of both cochlea and vestibulum. These findings implicated Fkh10 as an early regulator necessary for development of both cochlea

and vestibulum and identified its human homolog FKHL10 as a previously unknown candidate deafness gene at 5q34. The phenotype described by Hulander et al. (1998) resembles a group of human congenital inner ear malformations called 'common cavity.' Hulander et al. (1998) proposed that mutations in FKH10 may cause a 'common cavity' phenotype in humans.

[40126] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40127] Hulander, M.; Wurst, W.; Carlsson, P.; Enerback, S. : The winged helix transcription factor Fkh10 is required for normal development of the inner ear. Nature Genet. 20: 374–376, 1998. ; and

[40128] Larsson, C.; Hellqvist, M.; Pierrou, S.; White, I.; Enerback, S.; Carlsson, P. : Chromosomal localization of six human forkhead genes, freac–1 (FKHL5), –3 (FKHL7), –4 (FKHL8), –5 (FKHL9).

[40129] Further studies establishing the function and utilities of FOXI1 are found in John Hopkins OMIM database record ID 601093, and in cited publications numbered 9462–9460 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glycoprotein A

Repetitions Predominant (GARP, Accession NM_005512) is another VGAM1107 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12031, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40130] Another function of VGAM1107 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARP. RNA (guanine-7-) Methyltransferase (RNMT, Accession NM_003799) is another VGAM1107 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9883, to the nucleotide se-

quence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40131] Another function of VGAM1107 is therefore inhibition of RNA (guanine-7-) Methyltransferase (RNMT, Accession NM_003799), a gene which catalyzes the methylation of GpppN- at the guanine N7 position. Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Sphingosine Kinase 2 (SPHK2, Accession NM_020126) is another VGAM1107 host target gene. SPHK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPHK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPHK2 BINDING SITE, designated SEQ ID:21314, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40132] Another function of VGAM1107 is therefore inhibition of

Sphingosine Kinase 2 (SPHK2, Accession NM_020126). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPHK2. Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270) is another VGAM1107 host target gene. C20orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf20 BINDING SITE, designated SEQ ID:20247, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40133] Another function of VGAM1107 is therefore inhibition of Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf20. Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605) is another VGAM1107 host target gene. C5orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C5orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf6 BINDING SITE, designated SEQ ID:18706, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40134] Another function of VGAM1107 is therefore inhibition of Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf6. CAP350 (Accession NM_014810) is another VGAM1107 host target gene. CAP350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAP350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAP350 BINDING SITE, designated SEQ ID:16772, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40135] Another function of VGAM1107 is therefore inhibition of

CAP350 (Accession NM_014810). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAP350. Coactosin-like 1 (Dictyostelium) (COTL1, Accession XM_113840) is another VGAM1107 host target gene. COTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COTL1 BINDING SITE, designated SEQ ID:42468, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40136] Another function of VGAM1107 is therefore inhibition of Coactosin-like 1 (Dictyostelium) (COTL1, Accession XM_113840). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COTL1. FEM-2 (Accession NM_014634) is another VGAM1107 host target gene. FEM-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEM-2, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEM-2 BINDING SITE, designated SEQ ID:16007, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40137] Another function of VGAM1107 is therefore inhibition of FEM-2 (Accession NM_014634). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEM-2. FLJ10815 (Accession NM_018231) is another VGAM1107 host target gene. FLJ10815 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10815 BINDING SITE, designated SEQ ID:20169, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40138] Another function of VGAM1107 is therefore inhibition of FLJ10815 (Accession NM_018231). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10815. FLJ11783 (Accession NM_024891) is another VGAM1107 host target gene. FLJ11783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11783 BINDING SITE, designated SEQ ID:24366, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40139] Another function of VGAM1107 is therefore inhibition of FLJ11783 (Accession NM_024891). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11783. FLJ20105 (Accession NM_017669) is another VGAM1107 host target gene. FLJ20105 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20105, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20105 BINDING SITE, designated SEQ ID:19210, to the nucleotide

sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40140] Another function of VGAM1107 is therefore inhibition of FLJ20105 (Accession NM_017669). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20105. FLJ20477 (Accession NM_017837) is another VGAM1107 host target gene. FLJ20477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20477 BINDING SITE, designated SEQ ID:19504, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40141] Another function of VGAM1107 is therefore inhibition of FLJ20477 (Accession NM_017837). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20477. FLJ21736 (Accession NM_024922) is another VGAM1107 host target gene. FLJ21736 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ21736, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21736 BINDING SITE, designated SEQ ID:24458, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40142] Another function of VGAM1107 is therefore inhibition of FLJ21736 (Accession NM_024922). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21736. FLJ22009 (Accession XM_015700) is another VGAM1107 host target gene. FLJ22009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22009 BINDING SITE, designated SEQ ID:30245, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40143] Another function of VGAM1107 is therefore inhibition of FLJ22009 (Accession XM_015700). Accordingly, utilities of

VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22009. FLJ22419 (Accession NM_024697) is another VGAM1107 host target gene. FLJ22419 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22419, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22419 BINDING SITE, designated SEQ ID:24007, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40144] Another function of VGAM1107 is therefore inhibition of FLJ22419 (Accession NM_024697). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22419. H11 (Accession NM_014365) is another VGAM1107 host target gene. H11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by H11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H11 BINDING SITE, desig-

nated SEQ ID:15693, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40145] Another function of VGAM1107 is therefore inhibition of H11 (Accession NM_014365). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H11. Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571) is another VGAM1107 host target gene. HEYL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEYL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEYL BINDING SITE, designated SEQ ID:15928, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40146] Another function of VGAM1107 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEYL.

KIAA0016 (Accession NM_014765) is another VGAM1107 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16530, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40147] Another function of VGAM1107 is therefore inhibition of KIAA0016 (Accession NM_014765). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. PRO1048 (Accession NM_018497) is another VGAM1107 host target gene. PRO1048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1048 BINDING SITE, designated SEQ ID:20561, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM

RNA, also designated SEQ ID:3818.

[40148] Another function of VGAM1107 is therefore inhibition of PRO1048 (Accession NM_018497). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1048. Three Prime Repair Exonuclease 1 (TREX1, Accession NM_033627) is another VGAM1107 host target gene. TREX1 BINDING SITE1 and TREX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TREX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TREX1 BINDING SITE1 and TREX1 BINDING SITE2, designated SEQ ID:27340 and SEQ ID:27347 respectively, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40149] Another function of VGAM1107 is therefore inhibition of Three Prime Repair Exonuclease 1 (TREX1, Accession NM_033627). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TREX1. LOC143785 (Accession XM_084635) is another VGAM1107 host target

gene. LOC143785 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143785, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143785 BINDING SITE, designated SEQ ID:37632, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40150] Another function of VGAM1107 is therefore inhibition of LOC143785 (Accession XM_084635). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143785. LOC146714 (Accession XM_097072) is another VGAM1107 host target gene. LOC146714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146714 BINDING SITE, designated SEQ ID:40719, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40151] Another function of VGAM1107 is therefore inhibition of LOC146714 (Accession XM_097072). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146714. LOC149301 (Accession XM_086480) is another VGAM1107 host target gene. LOC149301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149301 BINDING SITE, designated SEQ ID:38692, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40152] Another function of VGAM1107 is therefore inhibition of LOC149301 (Accession XM_086480). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149301. LOC151277 (Accession XM_087155) is another VGAM1107 host target gene. LOC151277 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151277, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151277 BINDING SITE, designated SEQ ID:39094, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40153] Another function of VGAM1107 is therefore inhibition of LOC151277 (Accession XM_087155). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151277. LOC221486 (Accession XM_165760) is another VGAM1107 host target gene. LOC221486 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221486 BINDING SITE, designated SEQ ID:43742, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40154] Another function of VGAM1107 is therefore inhibition of LOC221486 (Accession XM_165760). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221486. LOC254205 (Accession XM_172962) is another VGAM1107 host target gene. LOC254205 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254205 BINDING SITE, designated SEQ ID:46219, to the nucleotide sequence of VGAM1107 RNA, herein designated VGAM RNA, also designated SEQ ID:3818.

[40155] Another function of VGAM1107 is therefore inhibition of LOC254205 (Accession XM_172962). Accordingly, utilities of VGAM1107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254205. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1108 (VGAM1108) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40156] VGAM1108 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1108 was detected is described hereinabove with reference to Figs. 1–8.

[40157] VGAM1108 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40158] VGAM1108 gene encodes a VGAM1108 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1108 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1108 precursor RNA is designated SEQ ID:1094, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1094 is located at position 30191 relative to the genome of Chimpanzee Cytomegalovirus.

[40159] VGAM1108 precursor RNA folds onto itself, forming VGAM1108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40160] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1108 folded precursor RNA into VGAM1108 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1108 RNA is designated SEQ ID:3819, and is provided hereinbelow with reference to the sequence listing part.

[40161] VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1108 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40162] VGAM1108 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1108 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1108 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[40163] The complementary binding of VGAM1108 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1108 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1108 host target RNA into VGAM1108 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40164] It is appreciated that VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1108 host target genes. The mRNA of each one of this plurality of VGAM1108 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1108 RNA, herein designated VGAM RNA, and which when bound by VGAM1108 RNA causes inhibition of translation of respective one or more VGAM1108 host target proteins.

[40165] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1108 gene, herein designated VGAM GENE, on one or more VGAM1108 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40166] It is yet further appreciated that a function of VGAM1108 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1108 correlate with, and may be deduced from, the identity of the host target genes which VGAM1108 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40167] Nucleotide sequences of the VGAM1108 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1108 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1108 are further described hereinbelow with reference to Table 1.

[40168] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1108 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1108 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40169] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1108 gene, herein designated VGAM is inhibition of expression of VGAM1108 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1108 correlate with, and may be deduced from, the identity of the target genes which VGAM1108 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40170] Potassium Inwardly-rectifying Channel, Subfamily J, Member 5 (KCNJ5, Accession NM_000890) is a VGAM1108 host target gene. KCNJ5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by KCNJ5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ5 BINDING SITE, designated SEQ ID:6587, to the nucleotide sequence of VGAM1108 RNA, herein designated VGAM RNA, also designated SEQ ID:3819.

[40171] A function of VGAM1108 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 5 (KCNJ5, Accession NM_000890), a gene which is a potassium inwardly-rectifying channel. Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ5. The function of KCNJ5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766.FLJ10352 (Accession NM_032142) is another VGAM1108 host target gene. FLJ10352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10352

BINDING SITE, designated SEQ ID:25826, to the nucleotide sequence of VGAM1108 RNA, herein designated VGAM RNA, also designated SEQ ID:3819.

[40172] Another function of VGAM1108 is therefore inhibition of FLJ10352 (Accession NM_032142). Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10352. KIAA0254 (Accession NM_014758) is another VGAM1108 host target gene. KIAA0254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0254 BINDING SITE, designated SEQ ID:16506, to the nucleotide sequence of VGAM1108 RNA, herein designated VGAM RNA, also designated SEQ ID:3819.

[40173] Another function of VGAM1108 is therefore inhibition of KIAA0254 (Accession NM_014758). Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0254. N4BP3 (Accession XM_038920) is another VGAM1108 host target gene. N4BP3 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32938, to the nucleotide sequence of VGAM1108 RNA, herein designated VGAM RNA, also designated SEQ ID:3819.

[40174] Another function of VGAM1108 is therefore inhibition of N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM1108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1109 (VGAM1109) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40175] VGAM1109 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1109 was detected is described hereinabove with reference to Figs. 1-8.

[40176] VGAM1109 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Chimpanzee Cytomegalovirus. VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40177] VGAM1109 gene encodes a VGAM1109 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1109 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1109 precursor RNA is designated SEQ ID:1095, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1095 is located at position 33182 relative to the genome of Chimpanzee Cytomegalovirus.

[40178] VGAM1109 precursor RNA folds onto itself, forming VGAM1109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40179] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1109 folded precursor RNA into VGAM1109 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1109 RNA is designated SEQ ID:3820, and is provided hereinbelow with reference to the sequence listing part.

[40180] VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1109 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40181] VGAM1109 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1109 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1109 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40182] The complementary binding of VGAM1109 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1109 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1109

host target RNA into VGAM1109 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40183] It is appreciated that VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1109 host target genes. The mRNA of each one of this plurality of VGAM1109 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1109 RNA, herein designated VGAM RNA, and which when bound by VGAM1109 RNA causes inhibition of translation of respective one or more VGAM1109 host target proteins.

[40184] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1109 gene, herein designated VGAM GENE, on one or more VGAM1109 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40185] It is yet further appreciated that a function of VGAM1109 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1109 include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGAM1109 correlate with, and may be deduced from, the identity of the host target genes which VGAM1109 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40186] Nucleotide sequences of the VGAM1109 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1109 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1109 are further

described hereinbelow with reference to Table 1.

[40187] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1109 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1109 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40188] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1109 gene, herein designated VGAM is inhibition of expression of VGAM1109 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1109 correlate with, and may be deduced from, the identity of the target genes which VGAM1109 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40189] Laminin, Beta 1 (LAMB1, Accession NM_002291) is a VGAM1109 host target gene. LAMB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LAMB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMB1 BIND-

ING SITE, designated SEQ ID:8072, to the nucleotide sequence of VGAM1109 RNA, herein designated VGAM RNA, also designated SEQ ID:3820.

[40190] A function of VGAM1109 is therefore inhibition of Laminin, Beta 1 (LAMB1, Accession NM_002291), a gene which mediates the attachment, migration, and organization of cells into tissues. Accordingly, utilities of VGAM1109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMB1. The function of LAMB1 has been established by previous studies. The major components of basal laminae are the glycoproteins laminin and collagen IV, both of which are heterotrimers. Laminin is a cruciform protein trimer of chains that when originally isolated from the extracellular matrix of tumor cells, were named A, B1, and B2, but were renamed alpha-1, beta-1, and gamma-1, respectively (Burgeson et al., 1994). The laminin and collagen IV isoforms vary from one basal lamina to another and are members of multigene families. These gene families (like others, such as the globins and myosins) may provide a means of generating functional diversity within a common structural framework. Modi et al. (1987) mapped the LAMB1 locus to 7q31.1-q31.3 by Southern blot analysis of

somatic cell hybrids and by in situ hybridization. On the other hand, by the same methods, Pikkarainen et al. (1987) placed LAMB1 in the 7q22 band. Jaye et al. (1987) regionalized LAMB1 to band 7q31 by somatic cell hybridization and in situ hybridization. Bonneau et al. (1991) described an infant with cutis laxa, emphysema, striking cardiac abnormalities and a diaphragmatic hernia leading to death at the age of 22 weeks. The infant had mild contractures at the elbows, hips, and knees, with bilateral hip dislocation. Arachnodactyly was striking. Chromosome studies showed a chromatid break at the junction of 7q31.3 and 7q32. Among 17 previously reported cases with the same syndrome, 1 was found to have a translocation involving 7q31 (Huret et al., 1991). Bonneau et al. (1991) called the condition neonatal cutis laxa with marfanoid phenotype. The clinical features and the location of the chromosomal change prompted Bonneau et al. (1991) to study laminin, which, by use of anti-human laminin antiserum, was found to be absent from the basement membranes of capillaries and the dermal-epidermal junction. Fibronectin was also not detected in the skin sample. Laminin B1 (OMIM Ref. No. 150240) maps to the same region of 7q. Bonneau et al. (1991) pointed to reports of

some 12 cases of neonatal 'Marfan syndrome' which might represent this same syndrome. These included the cases of Neimann et al. (1968), Hohn and Webb (1971), Lababidi and Monzon (1981), Buchanan and Wyatt (1985), Day and Burke (1986), and Gross et al. (1989). In a note added in proof, Bonneau et al. (1991) stated that studies of the case published by Neimann et al. (1968) showed deficiency of laminin in the basement membranes. Burgeson et al. (1994), a group of 14 leading researchers in the field of connective tissue proteins, adopted a new nomenclature for the laminins. They were numbered with arabic numerals in the order discovered. The previous A, B1, and B2 chains, and their isoforms, are alpha, beta, and gamma, respectively, followed by an arabic numeral to identify the isoform. For example, the first laminin identified from the Engelbreth-Holm-Swarm tumor (EHS) was designated laminin-1 with the chain composition alpha-1/beta-1/gamma-1. The genes for these 3 chains are LAMA1 (OMIM Ref. No. 150320), LAMB1, and LAMC1 (OMIM Ref. No. 150290).

[40191] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [40192] Burgeson, R. E.; Chiquet, M.; Deutzmann, R.; Ekblom, P.; Engel, J.; Kleinman, H.; Martin, G. R.; Meneguzzi, G.; Paulsson, M.; Sanes, J.; Timpl, R.; Tryggvason, K.; Yamada, Y.; Yurchenco, P. D. : A new nomenclature for the laminins. *Matrix Biol.* 14: 209–211, 1994. ; and
- [40193] Bonneau, D.; Huret, J. L.; Godeau, G.; Couet, D.; Putterman, M.; Tanzer, J.; Babin, P.; Larregue, M. : Recurrent *ctb(7)(q31.3)* and possible laminin involvement in a neonatal cutis laxa w.
- [40194] Further studies establishing the function and utilities of LAMB1 are found in John Hopkins OMIM database record ID 150240, and in cited publications numbered 11980–11998 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC90719 (Accession XM_033704) is another VGAM1109 host target gene. LOC90719 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90719 BINDING SITE, designated SEQ ID:31947, to the nucleotide sequence of VGAM1109 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3820.

[40195] Another function of VGAM1109 is therefore inhibition of LOC90719 (Accession XM_033704). Accordingly, utilities of VGAM1109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90719. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1110 (VGAM1110) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40196] VGAM1110 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1110 was detected is described hereinabove with reference to Figs. 1–8.

[40197] VGAM1110 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck Adenovirus 1. VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40198] VGAM1110 gene encodes a VGAM1110 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1110 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1110 precursor RNA is designated SEQ ID:1096, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1096 is located at position 8004 relative to the genome of Duck Adenovirus 1.

[40199] VGAM1110 precursor RNA folds onto itself, forming VGAM1110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40200] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1110 folded precursor RNA into VGAM1110 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1110 RNA is designated SEQ ID:3821, and is provided hereinbelow with reference to the sequence listing part.

[40201] VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1110 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40202] VGAM1110 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1110 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1110 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40203] The complementary binding of VGAM1110 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1110 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1110 host target RNA into VGAM1110 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40204] It is appreciated that VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1110 host target genes. The mRNA of

each one of this plurality of VGAM1110 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1110 RNA, herein designated VGAM RNA, and which when bound by VGAM1110 RNA causes inhibition of translation of respective one or more VGAM1110 host target proteins.

[40205] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1110 gene, herein designated VGAM GENE, on one or more VGAM1110 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[40206] It is yet further appreciated that a function of VGAM1110 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1110 include diagnosis, prevention and treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGAM1110 correlate with, and may be deduced from, the identity of the host target genes which VGAM1110 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40207] Nucleotide sequences of the VGAM1110 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1110 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1110 are further described hereinbelow with reference to Table 1.

[40208] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1110 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1110 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40209] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1110 gene, herein designated VGAM is inhibition of expression of VGAM1110 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1110 correlate with, and may be deduced from, the identity of the target genes which VGAM1110 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40210] Cytoplasmic FMR1 Interacting Protein 2 (CYFIP2, Accession XM_056963) is a VGAM1110 host target gene. CYFIP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYFIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYFIP2 BINDING SITE, designated SEQ ID:36439, to the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, also designated SEQ ID:3821.

[40211] A function of VGAM1110 is therefore inhibition of Cytoplasmic FMR1 Interacting Protein 2 (CYFIP2, Accession XM_056963). Accordingly, utilities of VGAM1110 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CYFIP2. Retinoic Acid Induced 14 (RAI14, Accession NM_015577) is another VGAM1110 host target gene. RAI14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI14 BINDING SITE, designated SEQ ID:17846, to the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, also designated SEQ ID:3821.

[40212] Another function of VGAM1110 is therefore inhibition of Retinoic Acid Induced 14 (RAI14, Accession NM_015577), a gene which is required for protein transport from the ER to the Golgi complex. Accordingly, utilities of VGAM1110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI14. The function of RAI14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1036. Tumor Protein P63 (TP63, Accession NM_003722) is another VGAM1110 host target gene.

TP63 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TP63, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP63 BINDING SITE, designated SEQ ID:9816, to the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, also designated SEQ ID:3821.

[40213] Another function of VGAM1110 is therefore inhibition of Tumor Protein P63 (TP63, Accession NM_003722). Accordingly, utilities of VGAM1110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP63. WW Domain Containing Oxidoreductase (WWOX, Accession NM_016373) is another VGAM1110 host target gene. WWOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WWOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WWOX BINDING SITE, designated SEQ ID:18504, to the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, also designated SEQ ID:3821.

[40214] Another function of VGAM1110 is therefore inhibition of WW Domain Containing Oxidoreductase (WWOX, Accession NM_016373), a gene which involves in protein-protein interactions and may contribute to the biologic consequences of DNA instability. Accordingly, utilities of VGAM1110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WWOX. The function of WWOX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644.DKFZP434N1511 (Accession XM_166138) is another VGAM1110 host target gene. DKFZP434N1511 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434N1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N1511 BINDING SITE, designated SEQ ID:43938, to the nucleotide sequence of VGAM1110 RNA, herein designated VGAM RNA, also designated SEQ ID:3821.

[40215] Another function of VGAM1110 is therefore inhibition of DKFZP434N1511 (Accession XM_166138). Accordingly,

utilities of VGAM1110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N1511. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1111 (VGAM1111) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40216] VGAM1111 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1111 was detected is described hereinabove with reference to Figs. 1-8.

[40217] VGAM1111 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40218] VGAM1111 gene encodes a VGAM1111 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1111 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1111 precursor RNA is designated SEQ ID:1097, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1097 is located at position 103122 relative to the genome of Camelpox Virus.

[40219] VGAM1111 precursor RNA folds onto itself, forming VGAM1111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40220] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1111 folded precursor RNA into VGAM1111 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1111 RNA is designated SEQ ID:3822, and

is provided hereinbelow with reference to the sequence listing part.

[40221] VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1111 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40222] VGAM1111 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1111 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1111 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40223] The complementary binding of VGAM1111 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1111 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1111 host target RNA into VGAM1111 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40224] It is appreciated that VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1111 host target genes. The mRNA of each one of this plurality of VGAM1111 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1111 RNA, herein designated VGAM RNA, and which when bound by VGAM1111 RNA causes inhibition of translation of respective one or more VGAM1111 host target proteins.

[40225] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1111 gene, herein designated VGAM GENE, on one or more VGAM1111 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40226] It is yet further appreciated that a function of VGAM1111 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1111 correlate with, and may be deduced from, the identity of the host target genes which VGAM1111 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40227] Nucleotide sequences of the VGAM1111 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1111 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1111 are further described hereinbelow with reference to Table 1.

[40228] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1111 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1111 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40229] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1111 gene, herein designated VGAM is inhibition of expression of VGAM1111 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1111 correlate with, and may be deduced from, the identity of the target genes which VGAM1111 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40230] ATPase, Ca++ Transporting, Type 2C, Member 1 (ATP2C1, Accession NM_014382) is a VGAM1111 host target gene. ATP2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP2C1 BINDING SITE, designated SEQ ID:15717, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40231] A function of VGAM1111 is therefore inhibition of ATPase, Ca++ Transporting, Type 2C, Member 1 (ATP2C1, Accession NM_014382). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP2C1. Go-

nadotropin-releasing Hormone Receptor (GNRHR, Accession NM_000406) is another VGAM1111 host target gene. GNRHR BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GNRHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNRHR BINDING SITE, designated SEQ ID:5982, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40232] Another function of VGAM1111 is therefore inhibition of Gonadotropin-releasing Hormone Receptor (GNRHR, Accession NM_000406), a gene which stimulates the secretionstimulates phosphoinositide turnover and membrane depolarization. Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNRHR. The function of GNRHR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM638. Mucin 3B (MUC3B, Accession XM_168578) is another VGAM1111 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 5` un-

translated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ ID:45256, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40233] Another function of VGAM1111 is therefore inhibition of Mucin 3B (MUC3B, Accession XM_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Polymerase (DNA directed) Sigma (POLS, Accession NM_006999) is another VGAM1111 host target gene. POLS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of POLS BINDING SITE, designated SEQ ID:13863, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40234] Another function of VGAM1111 is therefore inhibition of Polymerase (DNA directed) Sigma (POLS, Accession NM_006999), a gene which is necessary for chromosome segregation. Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLS. The function of POLS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM106.KIAA1161 (Accession XM_088501) is another VGAM1111 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39745, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40235] Another function of VGAM1111 is therefore inhibition of KIAA1161 (Accession XM_088501). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. Kelch-like 6 (Drosophila) (KLHL6, Accession NM_130446) is another VGAM1111 host target gene. KLHL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL6 BINDING SITE, designated SEQ ID:28213, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40236] Another function of VGAM1111 is therefore inhibition of Kelch-like 6 (Drosophila) (KLHL6, Accession NM_130446). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL6. RAS Protein Activator Like 2 (RASAL2, Accession NM_004841) is another VGAM1111 host target gene. RASAL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by RASAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASAL2 BINDING SITE, designated SEQ ID:11251, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40237] Another function of VGAM1111 is therefore inhibition of RAS Protein Activator Like 2 (RASAL2, Accession NM_004841). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASAL2. Small Nuclear RNA Activating Complex, Polypeptide 1, 43kDa (SNAPC1, Accession NM_003082) is another VGAM1111 host target gene. SNAPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAPC1 BINDING SITE, designated SEQ ID:9056, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40238] Another function of VGAM1111 is therefore inhibition of Small Nuclear RNA Activating Complex, Polypeptide 1, 43kDa (SNAPC1, Accession NM_003082). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAPC1. LOC149483 (Accession XM_086537) is another VGAM1111 host target gene. LOC149483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149483 BINDING SITE, designated SEQ ID:38757, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40239] Another function of VGAM1111 is therefore inhibition of LOC149483 (Accession XM_086537). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149483. LOC150397 (Accession XM_086907) is another VGAM1111 host target gene. LOC150397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150397, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150397 BINDING SITE, designated SEQ ID:38957, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40240] Another function of VGAM1111 is therefore inhibition of LOC150397 (Accession XM_086907). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150397. LOC152627 (Accession XM_087495) is another VGAM1111 host target gene. LOC152627 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39291, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40241] Another function of VGAM1111 is therefore inhibition of LOC152627 (Accession XM_087495). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152627. LOC219529 (Accession XM_167563) is another VGAM1111 host target gene. LOC219529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219529 BINDING SITE, designated SEQ ID:44672, to the nucleotide sequence of VGAM1111 RNA, herein designated VGAM RNA, also designated SEQ ID:3822.

[40242] Another function of VGAM1111 is therefore inhibition of LOC219529 (Accession XM_167563). Accordingly, utilities of VGAM1111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219529. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1112 (VGAM1112) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40243] VGAM1112 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1112 was detected is described hereinabove with reference to Figs. 1–8.

[40244] VGAM1112 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40245] VGAM1112 gene encodes a VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1112 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1112 precursor RNA is designated SEQ ID:1098, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1098 is located at position 103458 relative to the genome of Camelpox Virus.

[40246] VGAM1112 precursor RNA folds onto itself, forming VGAM1112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40247] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1112 folded precursor RNA into VGAM1112 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1112 RNA is designated SEQ ID:3823, and is provided hereinbelow with reference to the sequence listing part.

[40248] VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1112 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40249] VGAM1112 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1112 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1112 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40250] The complementary binding of VGAM1112 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1112 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1112 host target RNA into VGAM1112 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40251] It is appreciated that VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1112 host target genes. The mRNA of each one of this plurality of VGAM1112 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1112 RNA, herein designated VGAM RNA, and which when bound by VGAM1112 RNA causes inhibition of translation of respective one or more VGAM1112 host target proteins.

[40252] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1112 gene, herein designated VGAM GENE, on one or more VGAM1112 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40253] It is yet further appreciated that a function of VGAM1112 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1112 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1112 correlate with, and may be deduced from, the identity of the host target genes which VGAM1112 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40254] Nucleotide sequences of the VGAM1112 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1112 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1112 are further described hereinbelow with reference to Table 1.

[40255] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1112 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1112 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40256] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1112 gene, herein designated VGAM is inhibition of expression of VGAM1112 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1112 correlate with, and may be deduced from, the identity of the target genes which VGAM1112 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40257] DKFZP434J193 (Accession XM_048452) is a VGAM1112 host target gene. DKFZP434J193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by DKFZP434J193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J193 BINDING SITE, designated SEQ ID:35161, to the nucleotide sequence of VGAM1112 RNA, herein designated VGAM RNA, also designated SEQ ID:3823.

[40258] A function of VGAM1112 is therefore inhibition of DKFZP434J193 (Accession XM_048452). Accordingly, utilities of VGAM1112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J193. KIAA1548 (Accession NM_020909) is another VGAM1112 host target gene. KIAA1548 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1548, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1548 BINDING SITE, designated SEQ ID:21927, to the nucleotide sequence of VGAM1112 RNA, herein designated VGAM RNA, also designated SEQ ID:3823.

[40259] Another function of VGAM1112 is therefore inhibition of KIAA1548 (Accession NM_020909). Accordingly, utilities

of VGAM1112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1548. LOC150998 (Accession XM_097990) is another VGAM1112 host target gene. LOC150998 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150998, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150998 BINDING SITE, designated SEQ ID:41287, to the nucleotide sequence of VGAM1112 RNA, herein designated VGAM RNA, also designated SEQ ID:3823.

[40260] Another function of VGAM1112 is therefore inhibition of LOC150998 (Accession XM_097990). Accordingly, utilities of VGAM1112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150998. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1113 (VGAM1113) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40261] VGAM1113 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1113 was detected is described hereinabove with reference to Figs. 1–8.

[40262] VGAM1113 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40263] VGAM1113 gene encodes a VGAM1113 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1113 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1113 precursor RNA is designated SEQ ID:1099, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1099 is located at position 103649 relative to the genome of Camelpox Virus.

[40264] VGAM1113 precursor RNA folds onto itself, forming VGAM1113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40265] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1113 folded precursor RNA into VGAM1113 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1113 RNA is designated SEQ ID:3824, and is provided hereinbelow with reference to the sequence listing part.

[40266] VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1113 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[40267] VGAM1113 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1113 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1113 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40268] The complementary binding of VGAM1113 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1113 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1113 host target RNA into VGAM1113 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40269] It is appreciated that VGAM1113 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1113 host target genes. The mRNA of each one of this plurality of VGAM1113 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1113 RNA, herein designated VGAM RNA, and which when bound by VGAM1113 RNA causes inhibition of translation of respective one or more VGAM1113 host target proteins.

[40270] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1113 gene, herein designated VGAM GENE, on one or more VGAM1113 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40271] It is yet further appreciated that a function of VGAM1113 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1113 correlate with, and may be deduced from, the identity of the host target genes which VGAM1113 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40272] Nucleotide sequences of the VGAM1113 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1113 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1113 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1113 are further
described hereinbelow with reference to Table 1.

[40273] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1113 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1113 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[40274] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1113 gene, herein designated VGAM is
inhibition of expression of VGAM1113 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1113 correlate with, and may be deduced
from, the identity of the target genes which VGAM1113
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[40275] Adenylate Kinase 2 (AK2, Accession NM_013411) is a
VGAM1113 host target gene. AK2 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by AK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK2 BINDING SITE, designated SEQ ID:15075, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40276] A function of VGAM1113 is therefore inhibition of Adenylate Kinase 2 (AK2, Accession NM_013411), a gene which essential for maintenance and cell growth. Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK2. The function of AK2 has been established by previous studies. The existence of a second adenylate kinase (EC 2.7.4.3) locus linked to PGM1 and peptidase C, i.e., on chromosome 1, was suggested by cell hybridization studies by Van Cong et al. (1972). The Goss-Harris method of mapping combines features of recombinational study in families and syntenic tests in hybrid cells. As applied to chromosome 1, the method shows that AK2 and UMPK are distal to PGM1 and that the order of the loci is PGM1: UMPK: (AK2, alpha-FUC): ENO1 (Goss and Harris,

1977). Carritt et al. (1982) presented evidence that AK2 is in 1p34.

[40277] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40278] Goss, S. J.; Harris, H. : Gene transfer by means of cell fusion. II. The mapping of 8 loci on human chromosome 1 by statistical analysis of gene assortment in somatic cell hybrids. J. Cell Sci. 25: 39–57, 1977. ; and

[40279] Carritt, B.; King, J.; Welch, H. M. : Gene order and localization of enzyme loci on the short arm of chromosome 1. Ann. Hum. Genet. 46: 329–335, 1982.

[40280] Further studies establishing the function and utilities of AK2 are found in John Hopkins OMIM database record ID 103020, and in cited publications numbered 798–801 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calmodulin 2 (phosphorylase kinase, delta) (CALM2, Accession NM_001743) is another VGAM1113 host target gene. CALM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CALM2 BINDING SITE, designated SEQ ID:7480, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40281] Another function of VGAM1113 is therefore inhibition of Calmodulin 2 (phosphorylase kinase, delta) (CALM2, Accession NM_001743), a gene which mediates the control of a large number of enzymes by Ca^{++} . Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALM2. The function of CALM2 has been established by previous studies. McPherson et al. (1991) tentatively assigned the CALM2 gene to chromosome 10 by study of somatic cell hybrids. However, by PCR-based amplification of CALM2-specific sequences using DNA from human/hamster cell hybrids as template, Berchtold et al. (1993) found that the CALM2 gene is located on chromosome 2. They regionalized the gene to 2p21.3-p21.1 by in situ hybridization.

[40282] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40283] Berchtold, M. W.; Egli, R.; Rhyner, J. A.; Hameister, H.; Strehler, E. E. : Localization of the human bona fide calmodulin genes CALM1, CALM2, and CALM3 to chromosomes 14q24–q31, 2p21.1–p21.3, and 19q13.2–q13.3. Genomics 16: 461–465, 1993. ; and

[40284] McPherson, J. D.; Hickie, R. A.; Wasmuth, J. J.; Meyskens, F. L.; Perham, R. N.; Strehler, E. E.; Graham, M. T. : Chromosomal localization of multiple genes encoding calmodulin. (Abstra.

[40285] Further studies establishing the function and utilities of CALM2 are found in John Hopkins OMIM database record ID 114182, and in cited publications numbered 1257 and 12578 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hyaluronan-mediated Motility Receptor (RHAMM) (HMMR, Accession NM_012485) is another VGAM1113 host target gene. HMMR BINDING SITE1 and HMMR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HMMR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMMR BINDING SITE1 and HMMR BINDING SITE2, desig-

nated SEQ ID:14862 and SEQ ID:14860 respectively, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40286] Another function of VGAM1113 is therefore inhibition of Hyaluronan-mediated Motility Receptor (RHAMM) (HMMR, Accession NM_012485). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMMR. Myotubularin Related Protein 8 (MTMR8, Accession NM_015458) is another VGAM1113 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17741, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40287] Another function of VGAM1113 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1113 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379. Pentaxin-related Gene, Rapidly Induced By IL-1 Beta (PTX3, Accession NM_002852) is another VGAM1113 host target gene. PTX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTX3 BINDING SITE, designated SEQ ID:8747, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40288] Another function of VGAM1113 is therefore inhibition of Pentaxin-related Gene, Rapidly Induced By IL-1 Beta (PTX3, Accession NM_002852), a gene which is similar to the pentaxin subclass of inflammatory acute-phase proteins. Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTX3. The function of PTX3 and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM779. Chemokine (C-C motif) Receptor 7 (CCR7, Accession NM_001838) is another VGAM1113 host target gene. CCR7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR7 BINDING SITE, designated SEQ ID:7576, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40289] Another function of VGAM1113 is therefore inhibition of Chemokine (C-C motif) Receptor 7 (CCR7, Accession NM_001838). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR7. CCR4-NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM_013354) is another VGAM1113 host target gene. CNOT7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNOT7, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT7 BINDING SITE, designated SEQ ID:14998, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40290] Another function of VGAM1113 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM_013354). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT7. FLJ12363 (Accession NM_032167) is another VGAM1113 host target gene. FLJ12363 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12363 BINDING SITE, designated SEQ ID:25868, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40291] Another function of VGAM1113 is therefore inhibition of FLJ12363 (Accession NM_032167). Accordingly, utilities of

VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12363. FLJ13912 (Accession NM_022770) is another VGAM1113 host target gene. FLJ13912 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13912 BINDING SITE, designated SEQ ID:23025, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40292] Another function of VGAM1113 is therefore inhibition of FLJ13912 (Accession NM_022770). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13912. FLJ20340 (Accession NM_017773) is another VGAM1113 host target gene. FLJ20340 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20340

BINDING SITE, designated SEQ ID:19396, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40293] Another function of VGAM1113 is therefore inhibition of FLJ20340 (Accession NM_017773). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20340. FLJ21240 (Accession NM_024847) is another VGAM1113 host target gene. FLJ21240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21240 BINDING SITE, designated SEQ ID:24279, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40294] Another function of VGAM1113 is therefore inhibition of FLJ21240 (Accession NM_024847). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21240. FLJ23022 (Accession NM_025051) is another VGAM1113 host target gene. FLJ23022 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23022 BINDING SITE, designated SEQ ID:24647, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40295] Another function of VGAM1113 is therefore inhibition of FLJ23022 (Accession NM_025051). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23022. KIAA0748 (Accession NM_014796) is another VGAM1113 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16698, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40296] Another function of VGAM1113 is therefore inhibition of

KIAA0748 (Accession NM_014796). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. MCM10 Minichromosome Maintenance Deficient 10 (*S. cerevisiae*) (MCM10, Accession NM_018518) is another VGAM1113 host target gene. MCM10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCM10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCM10 BINDING SITE, designated SEQ ID:20594, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40297] Another function of VGAM1113 is therefore inhibition of MCM10 Minichromosome Maintenance Deficient 10 (*S. cerevisiae*) (MCM10, Accession NM_018518). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCM10. MGC15438 (Accession NM_032874) is another VGAM1113 host target gene. MGC15438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15438, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15438 BINDING SITE, designated SEQ ID:26693, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40298] Another function of VGAM1113 is therefore inhibition of MGC15438 (Accession NM_032874). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15438. MGC22014 (Accession XM_035307) is another VGAM1113 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32213, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40299] Another function of VGAM1113 is therefore inhibition of MGC22014 (Accession XM_035307). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC22014. Phorbol-12-myristate-13-acetate-induced Protein 1 (PMAIP1, Accession NM_021127) is another VGAM1113 host target gene. PMAIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMAIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMAIP1 BINDING SITE, designated SEQ ID:22098, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40300] Another function of VGAM1113 is therefore inhibition of Phorbol-12-myristate-13-acetate-induced Protein 1 (PMAIP1, Accession NM_021127). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMAIP1. Signal Sequence Receptor, Gamma (translocon-associated protein gamma) (SSR3, Accession NM_007107) is another VGAM1113 host target gene. SSR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSR3, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSR3 BINDING SITE, designated SEQ ID:13971, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40301] Another function of VGAM1113 is therefore inhibition of Signal Sequence Receptor, Gamma (translocon-associated protein gamma) (SSR3, Accession NM_007107). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSR3. T-box 21 (TBX21, Accession NM_013351) is another VGAM1113 host target gene. TBX21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBX21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX21 BINDING SITE, designated SEQ ID:14996, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40302] Another function of VGAM1113 is therefore inhibition of T-box 21 (TBX21, Accession NM_013351). Accordingly, utilities of VGAM1113 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with TBX21. LOC58489 (Accession XM_051862) is another VGAM1113 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35902, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40303] Another function of VGAM1113 is therefore inhibition of LOC58489 (Accession XM_051862). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC58489. LOC92267 (Accession XM_043979) is another VGAM1113 host target gene. LOC92267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92267 BINDING SITE, designated SEQ ID:34055, to the

nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40304] Another function of VGAM1113 is therefore inhibition of LOC92267 (Accession XM_043979). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92267. LOC92482 (Accession XM_045310) is another VGAM1113 host target gene. LOC92482 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92482 BINDING SITE, designated SEQ ID:34432, to the nucleotide sequence of VGAM1113 RNA, herein designated VGAM RNA, also designated SEQ ID:3824.

[40305] Another function of VGAM1113 is therefore inhibition of LOC92482 (Accession XM_045310). Accordingly, utilities of VGAM1113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92482. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1114 (VGAM1114) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40306] VGAM1114 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1114 was detected is described hereinabove with reference to Figs. 1-8.

[40307] VGAM1114 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40308] VGAM1114 gene encodes a VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1114 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1114 precursor RNA is designated SEQ ID:1100, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1100 is located at position 101465 relative to the genome of Camelpox Virus.

[40309] VGAM1114 precursor RNA folds onto itself, forming VGAM1114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40310] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1114 folded precursor RNA into VGAM1114 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1114 RNA is designated SEQ ID:3825, and is provided hereinbelow with reference to the sequence listing part.

[40311] VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1114 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1114 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40312] VGAM1114 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1114 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1114 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40313] The complementary binding of VGAM1114 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1114 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1114 host target RNA into VGAM1114 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40314] It is appreciated that VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1114 host target genes. The mRNA of each one of this plurality of VGAM1114 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1114 RNA, herein designated VGAM RNA, and which when bound by VGAM1114 RNA causes inhibition of translation of respective one or more VGAM1114 host target proteins.

[40315] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1114 gene, herein designated VGAM GENE, on one or more VGAM1114 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40316] It is yet further appreciated that a function of VGAM1114 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1114 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1114 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40317] Nucleotide sequences of the VGAM1114 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1114 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1114 are further described hereinbelow with reference to Table 1.

[40318] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1114 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1114 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40319] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1114 gene, herein designated VGAM is inhibition of expression of VGAM1114 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1114 correlate with, and may be deduced from, the identity of the target genes which VGAM1114

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40320] G Protein-coupled Receptor Kinase 7 (GPRK7, Accession NM_139209) is a VGAM1114 host target gene. GPRK7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPRK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRK7 BINDING SITE, designated SEQ ID:29226, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40321] A function of VGAM1114 is therefore inhibition of G Protein-coupled Receptor Kinase 7 (GPRK7, Accession NM_139209), a gene which may play a role in signal transduction pathways that involve calcium as a second messenger. Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRK7. The function of GPRK7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM640.Solute Carrier Family 12 (potassium/chloride

transporters), Member 7 (SLC12A7, Accession NM_006598) is another VGAM1114 host target gene. SLC12A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC12A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A7 BINDING SITE, designated SEQ ID:13372, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40322] Another function of VGAM1114 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598), a gene which is a potassium/chloride-cotransporter. Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A7. The function of SLC12A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM_003615) is another VGAM1114

host target gene. SLC4A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A7 BINDING SITE, designated SEQ ID:9667, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40323] Another function of VGAM1114 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM_003615), a gene which mediates the coupled movement of sodium and bicarbonate ions across the plasma membrane. Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A7. The function of SLC4A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM66.KIAA0391 (Accession NM_014672) is another VGAM1114 host target gene. KIAA0391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by KIAA0391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0391 BINDING SITE, designated SEQ ID:16134, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40324] Another function of VGAM1114 is therefore inhibition of KIAA0391 (Accession NM_014672). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0391. KIAA1884 (Accession XM_055539) is another VGAM1114 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36289, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40325] Another function of VGAM1114 is therefore inhibition of KIAA1884 (Accession XM_055539). Accordingly, utilities

of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. PP1201 (Accession NM_022152) is another VGAM1114 host target gene. PP1201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1201 BINDING SITE, designated SEQ ID:22709, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40326] Another function of VGAM1114 is therefore inhibition of PP1201 (Accession NM_022152). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1201. PRO0659 (Accession NM_014138) is another VGAM1114 host target gene. PRO0659 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0659

BINDING SITE, designated SEQ ID:15404, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40327] Another function of VGAM1114 is therefore inhibition of PRO0659 (Accession NM_014138). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0659. LOC148824 (Accession XM_097527) is another VGAM1114 host target gene. LOC148824 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148824 BINDING SITE, designated SEQ ID:40905, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40328] Another function of VGAM1114 is therefore inhibition of LOC148824 (Accession XM_097527). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148824. LOC203286 (Accession XM_117526) is another VGAM1114 host target gene. LOC203286 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43492, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40329] Another function of VGAM1114 is therefore inhibition of LOC203286 (Accession XM_117526). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. LOC221543 (Accession XM_168091) is another VGAM1114 host target gene. LOC221543 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221543, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221543 BINDING SITE, designated SEQ ID:45014, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40330] Another function of VGAM1114 is therefore inhibition of

LOC221543 (Accession XM_168091). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221543. LOC257596 (Accession XM_175296) is another VGAM1114 host target gene. LOC257596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257596 BINDING SITE, designated SEQ ID:46754, to the nucleotide sequence of VGAM1114 RNA, herein designated VGAM RNA, also designated SEQ ID:3825.

[40331] Another function of VGAM1114 is therefore inhibition of LOC257596 (Accession XM_175296). Accordingly, utilities of VGAM1114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257596. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1115 (VGAM1115) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[40332] VGAM1115 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1115 was detected is described hereinabove with reference to Figs. 1–8.

[40333] VGAM1115 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40334] VGAM1115 gene encodes a VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1115 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1115 precursor RNA is designated SEQ ID:1101, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1101 is located at position 100938 relative to the genome of Camelpox Virus.

[40335] VGAM1115 precursor RNA folds onto itself, forming VGAM1115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40336] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1115 folded precursor RNA into VGAM1115 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1115 RNA is designated SEQ ID:3826, and is provided hereinbelow with reference to the sequence listing part.

[40337] VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1115 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40338] VGAM1115 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1115 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1115 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[40339] The complementary binding of VGAM1115 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1115 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1115 host target RNA into VGAM1115 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40340] It is appreciated that VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1115 host target genes. The mRNA of each one of this plurality of VGAM1115 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1115 RNA, herein designated VGAM RNA, and which when bound by VGAM1115 RNA causes inhibition of translation of respective one or more VGAM1115 host target proteins.

[40341] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1115 gene, herein designated VGAM GENE, on one

or more VGAM1115 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40342] It is yet further appreciated that a function of VGAM1115 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1115 correlate with, and may be deduced from, the identity of the host target genes which VGAM1115 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40343] Nucleotide sequences of the VGAM1115 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1115 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1115 are further described hereinbelow with reference to Table 1.

[40344] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1115 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1115 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40345] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1115 gene, herein designated VGAM is inhibition of expression of VGAM1115 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1115 correlate with, and may be deduced from, the identity of the target genes which VGAM1115 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40346] Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-

3 receptor) (ITGA3, Accession NM_002204) is a VGAM1115 host target gene. ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ITGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA3 BINDING SITE1 and ITGA3 BINDING SITE2, designated SEQ ID:7964 and SEQ ID:12007 respectively, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40347] A function of VGAM1115 is therefore inhibition of Integrin, Alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3, Accession NM_002204), a gene which is a receptor for fibronectin, laminin, collagen, epiligrin and thrombospondin. Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA3. The function of ITGA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1020.BSPECV (Accession NM_016642) is another

VGAM1115 host target gene. BSPECV BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BSPECV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BSPECV BINDING SITE, designated SEQ ID:18748, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40348] Another function of VGAM1115 is therefore inhibition of BSPECV (Accession NM_016642). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BSPECV. Calpain 6 (CAPN6, Accession NM_014289) is another VGAM1115 host target gene. CAPN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN6 BINDING SITE, designated SEQ ID:15571, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40349] Another function of VGAM1115 is therefore inhibition of Calpain 6 (CAPN6, Accession NM_014289). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN6. HRD1 (Accession XM_045498) is another VGAM1115 host target gene. HRD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRD1 BINDING SITE, designated SEQ ID:34474, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40350] Another function of VGAM1115 is therefore inhibition of HRD1 (Accession XM_045498). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRD1. KIAA0293 (Accession XM_027045) is another VGAM1115 host target gene. KIAA0293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0293 BINDING SITE, designated SEQ ID:30394, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40351] Another function of VGAM1115 is therefore inhibition of KIAA0293 (Accession XM_027045). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0293. KIAA0712 (Accession NM_014715) is another VGAM1115 host target gene. KIAA0712 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0712 BINDING SITE, designated SEQ ID:16266, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40352] Another function of VGAM1115 is therefore inhibition of KIAA0712 (Accession NM_014715). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0712. KIAA0889 (Accession NM_015377) is another VGAM1115 host target gene. KIAA0889 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0889, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0889 BINDING SITE, designated SEQ ID:17675, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40353] Another function of VGAM1115 is therefore inhibition of KIAA0889 (Accession NM_015377). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0889. KIAA1853 (Accession XM_045184) is another VGAM1115 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34384, to the nucleotide sequence of VGAM1115 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3826.

[40354] Another function of VGAM1115 is therefore inhibition of KIAA1853 (Accession XM_045184). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1853. MGC1842 (Accession XM_037797) is another VGAM1115 host target gene. MGC1842 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC1842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1842 BINDING SITE, designated SEQ ID:32686, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40355] Another function of VGAM1115 is therefore inhibition of MGC1842 (Accession XM_037797). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1842. MGC20460 (Accession NM_053043) is another VGAM1115 host target gene. MGC20460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20460, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20460 BINDING SITE, designated SEQ ID:27588, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40356] Another function of VGAM1115 is therefore inhibition of MGC20460 (Accession NM_053043). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20460. MIDORI (Accession XM_057651) is another VGAM1115 host target gene. MIDORI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIDORI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIDORI BINDING SITE, designated SEQ ID:36527, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40357] Another function of VGAM1115 is therefore inhibition of MIDORI (Accession XM_057651). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MI-DORI. PRO2533 (Accession NM_018629) is another VGAM1115 host target gene. PRO2533 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2533 BINDING SITE, designated SEQ ID:20701, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40358] Another function of VGAM1115 is therefore inhibition of PRO2533 (Accession NM_018629). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2533. Zinc Finger Protein 384 (ZNF384, Accession NM_133476) is another VGAM1115 host target gene. ZNF384 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF384, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF384 BINDING SITE, designated SEQ

ID:28546, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40359] Another function of VGAM1115 is therefore inhibition of Zinc Finger Protein 384 (ZNF384, Accession NM_133476). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF384. LOC147976 (Accession XM_085980) is another VGAM1115 host target gene. LOC147976 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147976 BINDING SITE, designated SEQ ID:38428, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40360] Another function of VGAM1115 is therefore inhibition of LOC147976 (Accession XM_085980). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147976. LOC153565 (Accession XM_087713) is an-

other VGAM1115 host target gene. LOC153565 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153565 BINDING SITE, designated SEQ ID:39402, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40361] Another function of VGAM1115 is therefore inhibition of LOC153565 (Accession XM_087713). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153565. LOC202908 (Accession XM_114602) is another VGAM1115 host target gene. LOC202908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202908 BINDING SITE, designated SEQ ID:42995, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40362] Another function of VGAM1115 is therefore inhibition of LOC202908 (Accession XM_114602). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202908. LOC222057 (Accession XM_166594) is another VGAM1115 host target gene. LOC222057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222057 BINDING SITE, designated SEQ ID:44571, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40363] Another function of VGAM1115 is therefore inhibition of LOC222057 (Accession XM_166594). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222057. LOC255975 (Accession XM_171083) is another VGAM1115 host target gene. LOC255975 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255975, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255975 BINDING SITE, designated SEQ ID:45888, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40364] Another function of VGAM1115 is therefore inhibition of LOC255975 (Accession XM_171083). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255975. LOC256878 (Accession XM_173042) is another VGAM1115 host target gene. LOC256878 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256878 BINDING SITE, designated SEQ ID:46306, to the nucleotide sequence of VGAM1115 RNA, herein designated VGAM RNA, also designated SEQ ID:3826.

[40365] Another function of VGAM1115 is therefore inhibition of LOC256878 (Accession XM_173042). Accordingly, utilities of VGAM1115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC256878. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1116 (VGAM1116) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40366] VGAM1116 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1116 was detected is described hereinabove with reference to Figs. 1–8.

[40367] VGAM1116 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40368] VGAM1116 gene encodes a VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1116 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1116 precursor RNA is designated SEQ ID:1102, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1102 is located at position 49513 relative to the genome of Monkeypox Virus.

[40369] VGAM1116 precursor RNA folds onto itself, forming VGAM1116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40370] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1116 folded precursor RNA into VGAM1116 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1116 RNA is designated SEQ ID:3827, and is provided hereinbelow with reference to the sequence listing part.

[40371] VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1116 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40372] VGAM1116 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1116 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1116 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[40373] The complementary binding of VGAM1116 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1116 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1116 host target RNA into VGAM1116 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40374] It is appreciated that VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1116 host target genes. The mRNA of each one of this plurality of VGAM1116 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1116 RNA, herein designated VGAM RNA, and which when bound by VGAM1116 RNA causes

inhibition of translation of respective one or more VGAM1116 host target proteins.

[40375] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1116 gene, herein designated VGAM GENE, on one or more VGAM1116 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40376] It is yet further appreciated that a function of VGAM1116 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1116 include diagnosis, prevention and

treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1116 correlate with, and may be deduced from, the identity of the host target genes which VGAM1116 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40377] Nucleotide sequences of the VGAM1116 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1116 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1116 are further described hereinbelow with reference to Table 1.

[40378] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1116 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1116 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40379] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1116 gene, herein designated VGAM is inhibition of expression of VGAM1116 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1116 correlate with, and may be deduced from, the identity of the target genes which VGAM1116 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40380] HBP1 (Accession NM_012257) is a VGAM1116 host target gene. HBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HBP1 BINDING SITE, designated SEQ ID:14564, to the nucleotide sequence of VGAM1116 RNA, herein designated VGAM RNA, also designated SEQ ID:3827.

[40381] A function of VGAM1116 is therefore inhibition of HBP1 (Accession NM_012257). Accordingly, utilities of VGAM1116 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HBP1. PSR (Accession XM_036784) is another VGAM1116 host target gene. PSR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PSR BINDING SITE, designated SEQ ID:32500, to the nucleotide sequence of VGAM1116 RNA, herein designated VGAM RNA, also designated SEQ ID:3827.

[40382] Another function of VGAM1116 is therefore inhibition of PSR (Accession XM_036784). Accordingly, utilities of VGAM1116 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSR. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1117 (VGAM1117) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40383] VGAM1117 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1117 was detected is described hereinabove with reference to Figs. 1–8.

[40384] VGAM1117 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40385] VGAM1117 gene encodes a VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1117 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1117 precursor RNA is designated SEQ ID:1103, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1103 is located at position 45352 relative to the genome of Monkeypox Virus.

[40386] VGAM1117 precursor RNA folds onto itself, forming VGAM1117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40387] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1117 folded precursor RNA into VGAM1117 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1117 RNA is designated SEQ ID:3828, and is provided hereinbelow with reference to the sequence listing part.

[40388] VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1117 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40389] VGAM1117 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1117 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1117 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40390] The complementary binding of VGAM1117 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1117 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1117 host target RNA into VGAM1117 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40391] It is appreciated that VGAM1117 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1117 host target genes. The mRNA of each one of this plurality of VGAM1117 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1117 RNA, herein designated VGAM RNA, and which when bound by VGAM1117 RNA causes inhibition of translation of respective one or more VGAM1117 host target proteins.

[40392] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1117 gene, herein designated VGAM GENE, on one or more VGAM1117 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[40393] It is yet further appreciated that a function of VGAM1117 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1117 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1117 correlate with, and may be deduced from, the identity of the host target genes which VGAM1117 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40394] Nucleotide sequences of the VGAM1117 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1117 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1117 are further described hereinbelow with reference to Table 1.

[40395] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1117 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1117 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40396] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1117 gene, herein designated VGAM is inhibition of expression of VGAM1117 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1117 correlate with, and may be deduced from, the identity of the target genes which VGAM1117 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40397] KIAA1841 (Accession XM_087056) is a VGAM1117 host target gene. KIAA1841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1841 BINDING SITE, designated SEQ ID:39025, to the nucleotide sequence of VGAM1117 RNA, herein designated VGAM RNA, also designated SEQ ID:3828.

[40398] A function of VGAM1117 is therefore inhibition of

KIAA1841 (Accession XM_087056). Accordingly, utilities of VGAM1117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1841. LOC150468 (Accession XM_086926) is another VGAM1117 host target gene. LOC150468 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150468 BINDING SITE, designated SEQ ID:38974, to the nucleotide sequence of VGAM1117 RNA, herein designated VGAM RNA, also designated SEQ ID:3828.

[40399] Another function of VGAM1117 is therefore inhibition of LOC150468 (Accession XM_086926). Accordingly, utilities of VGAM1117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150468. LOC54557 (Accession XM_052961) is another VGAM1117 host target gene. LOC54557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC54557 BINDING SITE, designated SEQ ID:36054, to the nucleotide sequence of VGAM1117 RNA, herein designated VGAM RNA, also designated SEQ ID:3828.

[40400] Another function of VGAM1117 is therefore inhibition of LOC54557 (Accession XM_052961). Accordingly, utilities of VGAM1117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54557. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1118 (VGAM1118) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40401] VGAM1118 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1118 was detected is described hereinabove with reference to Figs. 1–8.

[40402] VGAM1118 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[40403] VGAM1118 gene encodes a VGAM1118 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1118 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1118 precursor RNA is designated SEQ ID:1104, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1104 is located at position 45554 relative to the genome of Monkeypox Virus.

[40404] VGAM1118 precursor RNA folds onto itself, forming VGAM1118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40405] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1118 folded precursor RNA into VGAM1118 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1118 RNA is designated SEQ ID:3829, and is provided hereinbelow with reference to the sequence listing part.

[40406] VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1118 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40407] VGAM1118 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1118 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1118 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40408] The complementary binding of VGAM1118 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1118 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1118 host target RNA into VGAM1118 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40409] It is appreciated that VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1118 host target genes. The mRNA of each one of this plurality of VGAM1118 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1118 RNA, herein designated VGAM RNA, and which when bound by VGAM1118 RNA causes inhibition of translation of respective one or more VGAM1118 host target proteins.

[40410] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1118 gene, herein designated VGAM GENE, on one or more VGAM1118 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40411] It is yet further appreciated that a function of VGAM1118 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1118 correlate with, and may be deduced from, the identity of the host target genes which VGAM1118 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40412] Nucleotide sequences of the VGAM1118 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1118 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1118 are further described hereinbelow with reference to Table 1.

[40413] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1118 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1118 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40414] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1118 gene, herein designated VGAM is inhibition of expression of VGAM1118 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1118 correlate with, and may be deduced from, the identity of the target genes which VGAM1118 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40415] Sulfotransferase Family, Cytosolic, 1C, Member 1 (SULT1C1, Accession NM_001056) is a VGAM1118 host target gene. SULT1C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SULT1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SULT1C1 BINDING SITE, designated SEQ ID:6718, to the nucleotide sequence of VGAM1118 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3829.

[40416] A function of VGAM1118 is therefore inhibition of Sulfo-transferase Family, Cytosolic, 1C, Member 1 (SULT1C1, Accession NM_001056). Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SULT1C1. Chromosome X Open Reading Frame 1 (CXorf1, Accession NM_004709) is another VGAM1118 host target gene. CXorf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf1 BINDING SITE, designated SEQ ID:11052, to the nucleotide sequence of VGAM1118 RNA, herein designated VGAM RNA, also designated SEQ ID:3829.

[40417] Another function of VGAM1118 is therefore inhibition of Chromosome X Open Reading Frame 1 (CXorf1, Accession NM_004709). Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf1. KIAA1211 (Accession XM_044178) is another VGAM1118 host target

gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1211 BINDING SITE, designated SEQ ID:34164, to the nucleotide sequence of VGAM1118 RNA, herein designated VGAM RNA, also designated SEQ ID:3829.

[40418] Another function of VGAM1118 is therefore inhibition of KIAA1211 (Accession XM_044178). Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373) is another VGAM1118 host target gene. SH3BGRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL BINDING SITE, designated SEQ ID:31022, to the nucleotide sequence of VGAM1118 RNA, herein designated VGAM

RNA, also designated SEQ ID:3829.

[40419] Another function of VGAM1118 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like (SH3BGRL, Accession XM_030373). Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL. LOC221143 (Accession XM_167986) is another VGAM1118 host target gene. LOC221143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221143 BINDING SITE, designated SEQ ID:44940, to the nucleotide sequence of VGAM1118 RNA, herein designated VGAM RNA, also designated SEQ ID:3829.

[40420] Another function of VGAM1118 is therefore inhibition of LOC221143 (Accession XM_167986). Accordingly, utilities of VGAM1118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221143. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1119 (VGAM1119) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40421] VGAM1119 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1119 was detected is described hereinabove with reference to Figs. 1–8.

[40422] VGAM1119 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40423] VGAM1119 gene encodes a VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1119 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1119 precursor RNA is designated SEQ ID:1105, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1105 is located at position 49470 relative to the genome of Camelpox Virus.

[40424] VGAM1119 precursor RNA folds onto itself, forming VGAM1119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40425] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1119 folded precursor RNA into VGAM1119 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1119 RNA is designated SEQ ID:3830, and is provided hereinbelow with reference to the sequence listing part.

[40426] VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1119 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1119 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40427] VGAM1119 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1119 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1119 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40428] The complementary binding of VGAM1119 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1119 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1119 host target RNA into VGAM1119 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40429] It is appreciated that VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1119 host target genes. The mRNA of each one of this plurality of VGAM1119 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1119 RNA, herein designated VGAM RNA, and which when bound by VGAM1119 RNA causes inhibition of translation of respective one or more VGAM1119 host target proteins.

[40430] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1119 gene, herein designated VGAM GENE, on one or more VGAM1119 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40431] It is yet further appreciated that a function of VGAM1119 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1119 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1119 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40432] Nucleotide sequences of the VGAM1119 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1119 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1119 are further described hereinbelow with reference to Table 1.

[40433] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1119 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1119 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40434] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1119 gene, herein designated VGAM is inhibition of expression of VGAM1119 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1119 correlate with, and may be deduced from, the identity of the target genes which VGAM1119

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40435] Collagen, Type VI, Alpha 1 (COL6A1, Accession NM_001848) is a VGAM1119 host target gene. COL6A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL6A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL6A1 BINDING SITE, designated SEQ ID:7583, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40436] A function of VGAM1119 is therefore inhibition of Collagen, Type VI, Alpha 1 (COL6A1, Accession NM_001848). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL6A1. Interleukin 15 Receptor, Alpha (IL15RA, Accession NM_002189) is another VGAM1119 host target gene. IL15RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL15RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL15RA BINDING SITE, designated SEQ ID:7945, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40437] Another function of VGAM1119 is therefore inhibition of Interleukin 15 Receptor, Alpha (IL15RA, Accession NM_002189), a gene which is essential for signal transduction. Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL15RA. The function of IL15RA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1103. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294) is another VGAM1119 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26062, to the nucleotide

sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40438] Another function of VGAM1119 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. KIAA1399 (Accession XM_046685) is another VGAM1119 host target gene. KIAA1399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1399 BINDING SITE, designated SEQ ID:34795, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40439] Another function of VGAM1119 is therefore inhibition of KIAA1399 (Accession XM_046685). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1399. LOC153937 (Accession XM_087813) is another VGAM1119 host target gene. LOC153937 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39442, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40440] Another function of VGAM1119 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153937. LOC222234 (Accession XM_168558) is another VGAM1119 host target gene. LOC222234 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222234, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222234 BINDING SITE, designated SEQ ID:45238, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40441] Another function of VGAM1119 is therefore inhibition of

LOC222234 (Accession XM_168558). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222234. LOC255565 (Accession XM_170811) is another VGAM1119 host target gene. LOC255565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255565 BINDING SITE, designated SEQ ID:45586, to the nucleotide sequence of VGAM1119 RNA, herein designated VGAM RNA, also designated SEQ ID:3830.

[40442] Another function of VGAM1119 is therefore inhibition of LOC255565 (Accession XM_170811). Accordingly, utilities of VGAM1119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255565. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1120 (VGAM1120) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[40443] VGAM1120 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1120 was detected is described hereinabove with reference to Figs. 1–8.

[40444] VGAM1120 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40445] VGAM1120 gene encodes a VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1120 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1120 precursor RNA is designated SEQ ID:1106, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1106 is located at position 44913 relative to the genome of Monkeypox Virus.

[40446] VGAM1120 precursor RNA folds onto itself, forming VGAM1120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40447] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1120 folded precursor RNA into VGAM1120 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1120 RNA is designated SEQ ID:3831, and is provided hereinbelow with reference to the sequence listing part.

[40448] VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1120 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40449] VGAM1120 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1120 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1120 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[40450] The complementary binding of VGAM1120 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1120 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1120 host target RNA into VGAM1120 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40451] It is appreciated that VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1120 host target genes. The mRNA of each one of this plurality of VGAM1120 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1120 RNA, herein designated VGAM RNA, and which when bound by VGAM1120 RNA causes inhibition of translation of respective one or more VGAM1120 host target proteins.

[40452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1120 gene, herein designated VGAM GENE, on one

or more VGAM1120 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40453] It is yet further appreciated that a function of VGAM1120 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1120 correlate with, and may be deduced from, the identity of the host target genes which VGAM1120 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40454] Nucleotide sequences of the VGAM1120 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1120 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1120 are further described hereinbelow with reference to Table 1.

[40455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1120 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1120 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40456] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1120 gene, herein designated VGAM is inhibition of expression of VGAM1120 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1120 correlate with, and may be deduced from, the identity of the target genes which VGAM1120 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40457] Fibroblast Growth Factor 5 (FGF5, Accession NM_004464)

is a VGAM1120 host target gene. FGF5 BINDING SITE1 and FGF5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGF5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF5 BINDING SITE1 and FGF5 BINDING SITE2, designated SEQ ID:10769 and SEQ ID:26996 respectively, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40458] A function of VGAM1120 is therefore inhibition of Fibroblast Growth Factor 5 (FGF5, Accession NM_004464), a gene which induces transformation and may regulate neuronal differentiation. Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF5. The function of FGF5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is another VGAM1120 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12884, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40459] Another function of VGAM1120 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117.FLJ10996 (Accession NM_019044) is another VGAM1120 host target gene. FLJ10996 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ10996 BINDING SITE, designated SEQ ID:21127, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40460] Another function of VGAM1120 is therefore inhibition of FLJ10996 (Accession NM_019044). Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10996. LOC146713 (Accession XM_097071) is another VGAM1120 host target gene. LOC146713 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146713 BINDING SITE, designated SEQ ID:40715, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40461] Another function of VGAM1120 is therefore inhibition of LOC146713 (Accession XM_097071). Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146713. LOC150271 (Accession XM_097859) is an-

other VGAM1120 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41170, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40462] Another function of VGAM1120 is therefore inhibition of LOC150271 (Accession XM_097859). Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC199926 (Accession XM_117157) is another VGAM1120 host target gene. LOC199926 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199926 BINDING SITE, designated SEQ ID:43260, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40463] Another function of VGAM1120 is therefore inhibition of LOC199926 (Accession XM_117157). Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199926. LOC202316 (Accession XM_117380) is another VGAM1120 host target gene. LOC202316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202316 BINDING SITE, designated SEQ ID:43425, to the nucleotide sequence of VGAM1120 RNA, herein designated VGAM RNA, also designated SEQ ID:3831.

[40464] Another function of VGAM1120 is therefore inhibition of LOC202316 (Accession XM_117380). Accordingly, utilities of VGAM1120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202316. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1121 (VGAM1121) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[40465] VGAM1121 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1121 was detected is described hereinabove with reference to Figs. 1-8.

[40466] VGAM1121 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40467] VGAM1121 gene encodes a VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1121 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1121 precursor RNA is designated SEQ ID:1107, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1107 is located at position 47689 relative to the genome of Saimiriine Herpesvirus 2.

[40468] VGAM1121 precursor RNA folds onto itself, forming VGAM1121 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40469] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1121 folded precursor RNA into VGAM1121 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1121 RNA is designated SEQ ID:3832, and is provided hereinbelow with reference to the sequence listing part.

[40470] VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1121 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40471] VGAM1121 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1121 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1121 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40472] The complementary binding of VGAM1121 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1121 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1121 host target RNA into VGAM1121 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40473] It is appreciated that VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1121 host target genes. The mRNA of each one of this plurality of VGAM1121 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1121 RNA, herein designated VGAM RNA, and which when bound by VGAM1121 RNA causes inhibition of translation of respective one or more VGAM1121 host target proteins.

[40474] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1121 gene, herein designated VGAM GENE, on one or more VGAM1121 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40475] It is yet further appreciated that a function of VGAM1121 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1121 correlate with, and may be deduced from, the identity of the host target genes which VGAM1121 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[40476] Nucleotide sequences of the VGAM1121 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1121 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1121 are further described hereinbelow with reference to Table 1.

[40477] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1121 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1121 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40478] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1121 gene, herein designated VGAM is inhibition of expression of VGAM1121 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1121 correlate with, and may be deduced from, the identity of the target genes which VGAM1121 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40479] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 1 (ADAMTS1, Accession NM_006988) is a VGAM1121 host target gene. ADAMTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS1 BINDING SITE, designated SEQ ID:13850, to the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, also designated SEQ ID:3832.

[40480] A function of VGAM1121 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 1 (ADAMTS1, Accession NM_006988). Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS1. ATPase, Cu⁺⁺ Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM_000053) is another VGAM1121 host target gene. ATP7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7B, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7B BINDING SITE, designated SEQ ID:5508, to the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, also designated SEQ ID:3832.

[40481] Another function of VGAM1121 is therefore inhibition of ATPase, Cu++ Transporting, Beta Polypeptide (Wilson disease) (ATP7B, Accession NM_000053). Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7B. BANK (Accession NM_017935) is another VGAM1121 host target gene. BANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANK BINDING SITE, designated SEQ ID:19623, to the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, also designated SEQ ID:3832.

[40482] Another function of VGAM1121 is therefore inhibition of BANK (Accession NM_017935). Accordingly, utilities of

VGAM1121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANK. Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117) is another VGAM1121 host target gene. KLHL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL4 BINDING SITE, designated SEQ ID:21197, to the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, also designated SEQ ID:3832.

[40483] Another function of VGAM1121 is therefore inhibition of Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117). Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL4. TEB4 (Accession XM_027156) is another VGAM1121 host target gene. TEB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEB4

BINDING SITE, designated SEQ ID:30428, to the nucleotide sequence of VGAM1121 RNA, herein designated VGAM RNA, also designated SEQ ID:3832.

[40484] Another function of VGAM1121 is therefore inhibition of TEB4 (Accession XM_027156). Accordingly, utilities of VGAM1121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEB4. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1122 (VGAM1122) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40485] VGAM1122 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1122 was detected is described hereinabove with reference to Figs. 1–8.

[40486] VGAM1122 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40487] VGAM1122 gene encodes a VGAM1122 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1122 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1122 precursor RNA is designated SEQ ID:1108, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1108 is located at position 43628 relative to the genome of Saimiriine Herpesvirus 2.

[40488] VGAM1122 precursor RNA folds onto itself, forming VGAM1122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40489] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1122 folded precursor RNA into VGAM1122 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1122 RNA is designated SEQ ID:3833, and is provided hereinbelow with reference to the sequence listing part.

[40490] VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1122 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40491] VGAM1122 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1122 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1122 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40492] The complementary binding of VGAM1122 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1122 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1122 host target RNA into VGAM1122 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40493] It is appreciated that VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1122 host target genes. The mRNA of each one of this plurality of VGAM1122 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1122 RNA, herein designated VGAM RNA, and which when bound by VGAM1122 RNA causes inhibition of translation of respective one or more VGAM1122 host target proteins.

[40494] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1122 gene, herein designated VGAM GENE, on one or more VGAM1122 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[40495] It is yet further appreciated that a function of VGAM1122 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1122 correlate with, and may be deduced from, the identity of the host target genes which VGAM1122 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40496] Nucleotide sequences of the VGAM1122 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1122 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1122 are further described hereinbelow with reference to Table 1.

[40497] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1122 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1122 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40498] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1122 gene, herein designated VGAM is inhibition of expression of VGAM1122 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1122 correlate with, and may be deduced from, the identity of the target genes which VGAM1122 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40499] Calumenin (CALU, Accession NM_001219) is a VGAM1122 host target gene. CALU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALU BINDING SITE, designated SEQ ID:6882, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40500] A function of VGAM1122 is therefore inhibition of Calumenin (CALU, Accession NM_001219), a gene which binds

7 calcium ions with a low affinity with unidentified function. Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALU. The function of CALU and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM253. V-raf-1 Murine Leukemia Viral Oncogene Homolog 1 (RAF1, Accession XM_087425) is another VGAM1122 host target gene. RAF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAF1 BINDING SITE, designated SEQ ID:39245, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40501] Another function of VGAM1122 is therefore inhibition of V-raf-1 Murine Leukemia Viral Oncogene Homolog 1 (RAF1, Accession XM_087425). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAF1. DKFZp761P1010 (Accession NM_018423) is another

VGAM1122 host target gene. DKFZp761P1010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761P1010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761P1010 BINDING SITE, designated SEQ ID:20477, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40502] Another function of VGAM1122 is therefore inhibition of DKFZp761P1010 (Accession NM_018423). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761P1010. HTMP10 (Accession NM_033207) is another VGAM1122 host target gene. HTMP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTMP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTMP10 BINDING SITE, designated SEQ ID:27049, to the nucleotide sequence of VGAM1122 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3833.

[40503] Another function of VGAM1122 is therefore inhibition of HTMP10 (Accession NM_033207). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTMP10. KIAA0471 (Accession NM_014857) is another VGAM1122 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16907, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40504] Another function of VGAM1122 is therefore inhibition of KIAA0471 (Accession NM_014857). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. KIAA1676 (Accession XM_167612) is another VGAM1122 host target gene. KIAA1676 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1676, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1676 BINDING SITE, designated SEQ ID:44726, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40505] Another function of VGAM1122 is therefore inhibition of KIAA1676 (Accession XM_167612). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1676. LOC115294 (Accession XM_054302) is another VGAM1122 host target gene. LOC115294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115294 BINDING SITE, designated SEQ ID:36143, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40506] Another function of VGAM1122 is therefore inhibition of LOC115294 (Accession XM_054302). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC115294. LOC121536 (Accession XM_058567) is another VGAM1122 host target gene. LOC121536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121536 BINDING SITE, designated SEQ ID:36664, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40507] Another function of VGAM1122 is therefore inhibition of LOC121536 (Accession XM_058567). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121536. LOC148936 (Accession XM_097556) is another VGAM1122 host target gene. LOC148936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148936 BINDING SITE, designated SEQ ID:40929, to

the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40508] Another function of VGAM1122 is therefore inhibition of LOC148936 (Accession XM_097556). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148936. LOC148938 (Accession XM_097555) is another VGAM1122 host target gene. LOC148938 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148938 BINDING SITE, designated SEQ ID:40922, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40509] Another function of VGAM1122 is therefore inhibition of LOC148938 (Accession XM_097555). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148938. LOC152674 (Accession XM_098251) is another VGAM1122 host target gene. LOC152674 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC152674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152674 BINDING SITE, designated SEQ ID:41536, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40510] Another function of VGAM1122 is therefore inhibition of LOC152674 (Accession XM_098251). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152674. LOC254100 (Accession XM_172851) is another VGAM1122 host target gene. LOC254100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254100 BINDING SITE, designated SEQ ID:46127, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40511] Another function of VGAM1122 is therefore inhibition of LOC254100 (Accession XM_172851). Accordingly, utilities

of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254100. LOC92249 (Accession XM_043814) is another VGAM1122 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34024, to the nucleotide sequence of VGAM1122 RNA, herein designated VGAM RNA, also designated SEQ ID:3833.

[40512] Another function of VGAM1122 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM1122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1123 (VGAM1123) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40513] VGAM1123 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1123 was detected is described hereinabove with reference to Figs. 1-8.

[40514] VGAM1123 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40515] VGAM1123 gene encodes a VGAM1123 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1123 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1123 precursor RNA is designated SEQ ID:1109, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1109 is located at position 45011 relative to the genome of Saimiriine Herpesvirus 2.

[40516] VGAM1123 precursor RNA folds onto itself, forming VGAM1123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40517] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1123 folded precursor RNA into VGAM1123 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1123 RNA is designated SEQ ID:3834, and is provided hereinbelow with reference to the sequence listing part.

[40518] VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1123 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[40519] VGAM1123 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1123 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1123 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40520] The complementary binding of VGAM1123 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1123 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1123 host target RNA into VGAM1123 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40521] It is appreciated that VGAM1123 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1123 host target genes. The mRNA of each one of this plurality of VGAM1123 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1123 RNA, herein designated VGAM RNA, and which when bound by VGAM1123 RNA causes inhibition of translation of respective one or more VGAM1123 host target proteins.

[40522] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1123 gene, herein designated VGAM GENE, on one or more VGAM1123 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40523] It is yet further appreciated that a function of VGAM1123 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1123 correlate with, and may be deduced from, the identity of the host target genes which VGAM1123 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40524] Nucleotide sequences of the VGAM1123 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1123 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1123 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1123 are further
described hereinbelow with reference to Table 1.

[40525] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1123 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1123 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[40526] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1123 gene, herein designated VGAM is
inhibition of expression of VGAM1123 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1123 correlate with, and may be deduced
from, the identity of the target genes which VGAM1123
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[40527] Caspase 2, Apoptosis-related Cysteine Protease (neural
precursor cell expressed, developmentally down-reg-

ulated 2) (CASP2, Accession NM_001224) is a VGAM1123 host target gene. CASP2 BINDING SITE1 through CASP2 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP2 BINDING SITE1 through CASP2 BINDING SITE4, designated SEQ ID:6890, SEQ ID:26853, SEQ ID:26858 and SEQ ID:26863 respectively, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40528] A function of VGAM1123 is therefore inhibition of Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_001224), a gene which involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP2. The function of CASP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM148.Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147) is another VGAM1123 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42720, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40529] Another function of VGAM1123 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120.FK506 Binding Protein 12-rapamycin Associated Protein 1 (FRAP1, Accession NM_004958) is another VGAM1123 host target gene. FRAP1 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FRAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRAP1 BINDING SITE, designated SEQ ID:11403, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40530] Another function of VGAM1123 is therefore inhibition of FK506 Binding Protein 12-rapamycin Associated Protein 1 (FRAP1, Accession NM_004958), a gene which acts as the target for the cell-cycle arrest and immunosuppressive effects of the fkbp12-rapamycin complex. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FRAP1. The function of FRAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM496. High-mobility Group 20A (HMG20A, Accession NM_018200) is another VGAM1123 host target gene. HMG20A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMG20A, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMG20A BINDING SITE, designated SEQ ID:20073, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40531] Another function of VGAM1123 is therefore inhibition of High-mobility Group 20A (HMG20A, Accession NM_018200). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMG20A. Reelin (RELN, Accession XM_168628) is another VGAM1123 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45280, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40532] Another function of VGAM1123 is therefore inhibition of Reelin (RELN, Accession XM_168628), a gene which regulates microtubule function in neurons and neuronal mi-

gration. Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35.DCOHM (Accession NM_032151) is another VGAM1123 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25842, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40533] Another function of VGAM1123 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. HTGN29 (Accession NM_020199) is another VGAM1123 host target gene. HTGN29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by HTGN29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTGN29 BINDING SITE, designated SEQ ID:21432, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40534] Another function of VGAM1123 is therefore inhibition of HTGN29 (Accession NM_020199). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTGN29. KIAA1728 (Accession XM_043492) is another VGAM1123 host target gene. KIAA1728 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1728 BINDING SITE, designated SEQ ID:33949, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40535] Another function of VGAM1123 is therefore inhibition of KIAA1728 (Accession XM_043492). Accordingly, utilities

of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1728. LOC145483 (Accession XM_085156) is another VGAM1123 host target gene. LOC145483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145483 BINDING SITE, designated SEQ ID:37879, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40536] Another function of VGAM1123 is therefore inhibition of LOC145483 (Accession XM_085156). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145483. LOC145757 (Accession XM_085227) is another VGAM1123 host target gene. LOC145757 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145757, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145757 BINDING SITE, designated SEQ ID:37967, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40537] Another function of VGAM1123 is therefore inhibition of LOC145757 (Accession XM_085227). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145757. LOC153883 (Accession XM_087798) is another VGAM1123 host target gene. LOC153883 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153883 BINDING SITE, designated SEQ ID:39429, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40538] Another function of VGAM1123 is therefore inhibition of LOC153883 (Accession XM_087798). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153883. LOC166793 (Accession NM_145291) is another VGAM1123 host target gene. LOC166793 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC166793, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166793 BINDING SITE, designated SEQ ID:29804, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40539] Another function of VGAM1123 is therefore inhibition of LOC166793 (Accession NM_145291). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166793. LOC219699 (Accession XM_172822) is another VGAM1123 host target gene. LOC219699 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC219699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219699 BINDING SITE, designated SEQ ID:46100, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40540] Another function of VGAM1123 is therefore inhibition of

LOC219699 (Accession XM_172822). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219699. LOC51054 (Accession NM_015899) is another VGAM1123 host target gene. LOC51054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51054 BINDING SITE, designated SEQ ID:18043, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40541] Another function of VGAM1123 is therefore inhibition of LOC51054 (Accession NM_015899). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51054. LOC51691 (Accession NM_016200) is another VGAM1123 host target gene. LOC51691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC51691 BINDING SITE, designated SEQ ID:18291, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40542] Another function of VGAM1123 is therefore inhibition of LOC51691 (Accession NM_016200). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51691. LOC90786 (Accession XM_034127) is another VGAM1123 host target gene. LOC90786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90786 BINDING SITE, designated SEQ ID:32015, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40543] Another function of VGAM1123 is therefore inhibition of LOC90786 (Accession XM_034127). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90786. LOC92465 (Accession XM_045250) is another

VGAM1123 host target gene. LOC92465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92465 BINDING SITE, designated SEQ ID:34393, to the nucleotide sequence of VGAM1123 RNA, herein designated VGAM RNA, also designated SEQ ID:3834.

[40544] Another function of VGAM1123 is therefore inhibition of LOC92465 (Accession XM_045250). Accordingly, utilities of VGAM1123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92465. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1124 (VGAM1124) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40545] VGAM1124 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1124 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[40546] VGAM1124 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40547] VGAM1124 gene encodes a VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1124 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1124 precursor RNA is designated SEQ ID:1110, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1110 is located at position 43302 relative to the genome of Saimiriine Herpesvirus 2.

[40548] VGAM1124 precursor RNA folds onto itself, forming VGAM1124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40549] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1124 folded precursor RNA into VGAM1124 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1124 RNA is designated SEQ ID:3835, and is provided hereinbelow with reference to the sequence listing part.

[40550] VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1124 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40551] VGAM1124 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1124 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1124 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1124 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40552] The complementary binding of VGAM1124 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1124 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1124 host target RNA into VGAM1124 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40553] It is appreciated that VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1124 host target genes. The mRNA of each one of this plurality of VGAM1124 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1124 RNA, herein designated VGAM RNA, and which when bound by VGAM1124 RNA causes inhibition of translation of respective one or more VGAM1124 host target proteins.

[40554] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1124 gene, herein designated VGAM GENE, on one or more VGAM1124 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40555] It is yet further appreciated that a function of VGAM1124 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1124 correlate with, and may be deduced from, the identity of the host target genes which VGAM1124 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40556] Nucleotide sequences of the VGAM1124 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1124 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1124 are further described hereinbelow with reference to Table 1.

[40557] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1124 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1124 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40558] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1124 gene, herein designated VGAM is inhibition of expression of VGAM1124 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1124 correlate with, and may be deduced from, the identity of the target genes which VGAM1124 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40559] DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681) is a VGAM1124 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16158, to the nucleotide sequence of VGAM1124 RNA, herein designated VGAM RNA, also designated SEQ ID:3835.

[40560] A function of VGAM1124 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681). Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. Endothelial Differentiation, Lysophosphatidic Acid G-protein-coupled Receptor, 2 (EDG2, Accession NM_057159) is another VGAM1124 host target gene. EDG2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EDG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDG2 BINDING SITE, designated SEQ ID:27669, to the nucleotide sequence of VGAM1124 RNA, herein designated VGAM RNA, also designated SEQ ID:3835.

[40561] Another function of VGAM1124 is therefore inhibition of

Endothelial Differentiation, Lysophosphatidic Acid G-protein-coupled Receptor, 2 (EDG2, Accession NM_057159). Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDG2. ICK (Accession NM_014920) is another VGAM1124 host target gene. ICK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICK BINDING SITE, designated SEQ ID:17191, to the nucleotide sequence of VGAM1124 RNA, herein designated VGAM RNA, also designated SEQ ID:3835.

[40562] Another function of VGAM1124 is therefore inhibition of ICK (Accession NM_014920). Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICK. LOC112687 (Accession XM_053145) is another VGAM1124 host target gene. LOC112687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112687, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112687 BINDING SITE, designated SEQ ID:36064, to the nucleotide sequence of VGAM1124 RNA, herein designated VGAM RNA, also designated SEQ ID:3835.

[40563] Another function of VGAM1124 is therefore inhibition of LOC112687 (Accession XM_053145). Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112687. LOC220692 (Accession XM_165991) is another VGAM1124 host target gene. LOC220692 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220692 BINDING SITE, designated SEQ ID:43831, to the nucleotide sequence of VGAM1124 RNA, herein designated VGAM RNA, also designated SEQ ID:3835.

[40564] Another function of VGAM1124 is therefore inhibition of LOC220692 (Accession XM_165991). Accordingly, utilities of VGAM1124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220692. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1125 (VGAM1125) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40565] VGAM1125 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1125 was detected is described hereinabove with reference to Figs. 1–8.

[40566] VGAM1125 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40567] VGAM1125 gene encodes a VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1125 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1125 precursor RNA is designated SEQ ID:1111, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1111 is located at position 42164 relative to the genome of Saimiriine Herpesvirus 2.

[40568] VGAM1125 precursor RNA folds onto itself, forming VGAM1125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40569] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1125 folded precursor RNA into VGAM1125 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1125 RNA is designated SEQ ID:3836, and is provided hereinbelow with reference to the sequence listing part.

[40570] VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1125 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40571] VGAM1125 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1125 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1125 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40572] The complementary binding of VGAM1125 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1125 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1125 host target RNA into VGAM1125 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40573] It is appreciated that VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1125 host target genes. The mRNA of each one of this plurality of VGAM1125 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1125 RNA, herein designated VGAM RNA, and which when bound by VGAM1125 RNA causes

inhibition of translation of respective one or more VGAM1125 host target proteins.

[40574] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1125 gene, herein designated VGAM GENE, on one or more VGAM1125 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40575] It is yet further appreciated that a function of VGAM1125 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1125 include diagnosis, prevention and

treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1125 correlate with, and may be deduced from, the identity of the host target genes which VGAM1125 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40576] Nucleotide sequences of the VGAM1125 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1125 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1125 are further described hereinbelow with reference to Table 1.

[40577] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1125 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1125 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40578] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1125 gene, herein designated VGAM is inhibition of expression of VGAM1125 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1125 correlate with, and may be deduced from, the identity of the target genes which VGAM1125 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40579] B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898) is a VGAM1125 host target gene. BCL11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL11B BINDING SITE, designated SEQ ID:23165, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40580] A function of VGAM1125 is therefore inhibition of B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11B. Collagen, Type IV, Alpha 4 (COL4A4, Accession NM_000092) is another VGAM1125 host target gene. COL4A4 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COL4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A4 BINDING SITE, designated SEQ ID:5550, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40581] Another function of VGAM1125 is therefore inhibition of Collagen, Type IV, Alpha 4 (COL4A4, Accession NM_000092). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A4. Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM_003633) is another VGAM1125 host target gene. ENC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ENC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENC1 BINDING SITE, designated SEQ ID:9699, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40582] Another function of VGAM1125 is therefore inhibition of Ectodermal–neural Cortex (with BTB–like domain) (ENC1, Accession NM_003633), a gene which is an actin–binding protein involved in the regulation of neuronal process formation and in differentiation of neural crest cells. Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENC1. The function of ENC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233. G Protein–coupled Receptor 23 (GPR23, Accession XM_018505) is another VGAM1125 host target gene. GPR23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR23 BINDING SITE, designated SEQ ID:30363, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40583] Another function of VGAM1125 is therefore inhibition of G Protein–coupled Receptor 23 (GPR23, Accession

XM_018505), a gene which is a member of the G protein-coupled receptor family. Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR23. The function of GPR23 has been established by previous studies. By searching the expressed sequence tag database, Janssens et al. (1997) found an EST bearing 63% amino-acid identity with the chicken P2Y(5) receptor. By high-stringency PCR using primers based on this EST, Janssens et al. (1997) isolated a complete clone from human genomic DNA. The sequence was 61% identical to the chicken P2Y(5) receptor and 30–33% identical to other P2Y subtypes. O'Dowd et al. (1997) mapped the GPR23 gene to Xq13–q21.1 by fluorescence in situ hybridization.

[40584] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40585] Janssens, R.; Boeynaems, J.–M.; Godart, M.; Communi, D. : Cloning of a human heptahelical receptor closely related to the P2Y(5) receptor. *Biochem. Biophys. Res. Commun.* 236: 106–112, 1997. ; and

[40586] O'Dowd, B. F.; Nguyen, T.; Jung, B. P.; Marchese, A.; Cheng, R.; Heng, H. H. Q.; Kolakowski, L. F., Jr.; Lynch, K.

R.; George, S. R. : Cloning and chromosomal mapping of four putative n.

[40587] Further studies establishing the function and utilities of GPR23 are found in John Hopkins OMIM database record ID 300086, and in cited publications numbered 10977–10978 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Src-like-adaptor 2 (SLA2, Accession NM_032214) is another VGAM1125 host target gene. SLA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLA2 BINDING SITE, designated SEQ ID:25942, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40588] Another function of VGAM1125 is therefore inhibition of Src-like-adaptor 2 (SLA2, Accession NM_032214). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLA2. Serine Racemase (SRR, Accession NM_021947) is another VGAM1125 host target gene. SRR

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRR BINDING SITE, designated SEQ ID:22476, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40589] Another function of VGAM1125 is therefore inhibition of Serine Racemase (SRR, Accession NM_021947). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRR. WSX1 (Accession NM_004843) is another VGAM1125 host target gene. WSX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WSX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WSX1 BINDING SITE, designated SEQ ID:11255, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40590] Another function of VGAM1125 is therefore inhibition of

WSX1 (Accession NM_004843), a gene which is a member of the class I cytokine receptor family and involved in the modulation of the immune response. Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WSX1. The function of WSX1 has been established by previous studies. CD4⁺ helper T cells differentiate into type 1 (Th1) cells, critical for cell-mediated immunity, predominantly under the influence of IL12 (OMIM Ref. No. 161560). IL4 (OMIM Ref. No. 147780) influences their differentiation into type 2 (Th2) cells, critical for most antibody responses. Mice deficient in these cytokines, their receptors, or associated transcription factors have impaired, but not absent, Th1 or Th2 immune responses. Sprecher et al. (1998) searched an EST database for sequences similar to the class I cytokine receptor gp130 (OMIM Ref. No. 600694). They identified a cDNA encoding a class I cytokine receptor, which they designated WSX1, from an infant brain cDNA library. Using a homology screen, Chen et al. (2000) identified TCCR (T-cell cytokine receptor), a type I cytokine receptor family member identical to WSX1 and most homologous (26% identity, 37% similarity) to IL12RB2 (OMIM Ref. No. 601642). By screen-

ing a peripheral blood leukocyte (PBL) library, Chen et al. (2000) isolated a full-length cDNA encoding a deduced 636-amino acid TCCR protein. Sequence analysis predicted a single transmembrane domain, a WSX signature motif, and 7 potential N-glycosylation sites in its extracellular domain, and a box1 motif in its intracellular region. Mouse Tccr, isolated from a spleen library, is 62% identical to the human sequence. Northern blot analysis revealed expression of a 3.5-kb transcript in human PBL, thymus, and spleen as well as in adult and fetal lung. Real-time PCR analysis of mouse splenocytes revealed highest expression in CD4⁺ T cells and in natural killer cells. Among CD4⁺ T cells, expression was highest in undifferentiated (Th0) cells, with reduced expression in Th1 and Th2 cells. Animal model experiments lend further support to the function of WSX1. Yoshida et al. (2001) generated mice deficient in *Wsx1* by homologous recombination. *Wsx1*-deficient mice were apparently normal and healthy. In vitro immunologic analysis showed that the *Wsx1* ^{-/-} mice had weak IFNG primary responses but normal secondary responses to mitogen compared with wild-type mice. In response to *Leishmania* infection, mice lacking *Wsx1* were more susceptible than wildtype mice and

had weak early IFNG responses. The footpads were enlarged with severe ulceration. The phenotype was not as severe as that of Balb-c mice. RT-PCR analysis indicated that high early IL4 levels were maintained in the knockout mice. Infection with the avirulent *Mycobacterium bovis* BCG resulted in numerous enlarged and poorly differentiated liver granulomas in *Wsx1* $-/-$ mice compared with wildtype. However, there was no significant difference in bacterial numbers or in liver damage as assessed by transaminase levels. Yoshida et al. (2001) concluded that the impact of lack of *Wsx1* early in response to infectious agents is significant, but the impact is mitigated by the presence of other cytokines, such as IFNG and IL12, and their receptors in later phases of the infection.

[40591] It is appreciated that the abovementioned animal model for *WSX1* is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[40592] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40593] Sprecher, C. A.; Grant, F. J.; Baumgartner, J. W.; Presnell, S. R.; Schrader, S. K.; Yamagiwa, T.; Whitmore, T. E.; O'Hara,

P. J.; Foster, D. F. : Cloning and characterization of a novel class I cytokine receptor. Biochem. Biophys. Res. Comm. 246: 82–90, 1998. ; and

[40594] Yoshida, H.; Hamano, S.; Senaldi, G.; Covey, T.; Faggioni, R.; Mu, S.; Xia, M.; Wakeham, A. C.; Nishina, H.; Potter, J.; Saris, C. J. M.; Mak, T. W. : WSX–1 is required for the initiation.

[40595] Further studies establishing the function and utilities of WSX1 are found in John Hopkins OMIM database record ID 605350, and in cited publications numbered 6180–6182 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Betaine–homocysteine Methyltransferase (BHMT, Accession NM_001713) is another VGAM1125 host target gene. BHMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHMT BINDING SITE, designated SEQ ID:7444, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40596] Another function of VGAM1125 is therefore inhibition of

Betaine-homocysteine Methyltransferase (BHMT, Accession NM_001713). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHMT. Chemokine (C-C motif) Receptor 5 (CCR5, Accession NM_000579) is another VGAM1125 host target gene. CCR5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR5 BINDING SITE, designated SEQ ID:6184, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40597] Another function of VGAM1125 is therefore inhibition of Chemokine (C-C motif) Receptor 5 (CCR5, Accession NM_000579). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR5. CEP3 (Accession NM_006449) is another VGAM1125 host target gene. CEP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEP3, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP3 BINDING SITE, designated SEQ ID:13159, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40598] Another function of VGAM1125 is therefore inhibition of CEP3 (Accession NM_006449). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP3. KIAA1948 (Accession XM_091984) is another VGAM1125 host target gene. KIAA1948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1948 BINDING SITE, designated SEQ ID:40080, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40599] Another function of VGAM1125 is therefore inhibition of KIAA1948 (Accession XM_091984). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1948. Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM_007150) is another VGAM1125 host target gene. ZNF185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF185 BINDING SITE, designated SEQ ID:14001, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40600] Another function of VGAM1125 is therefore inhibition of Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM_007150). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF185. LOC126964 (Accession XM_059100) is another VGAM1125 host target gene. LOC126964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126964 BINDING SITE, desig-

nated SEQ ID:36883, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40601] Another function of VGAM1125 is therefore inhibition of LOC126964 (Accession XM_059100). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126964. LOC150848 (Accession XM_097959) is another VGAM1125 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41250, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40602] Another function of VGAM1125 is therefore inhibition of LOC150848 (Accession XM_097959). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150848. LOC151248 (Accession XM_087143) is another VGAM1125 host target gene. LOC151248 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151248 BINDING SITE, designated SEQ ID:39083, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40603] Another function of VGAM1125 is therefore inhibition of LOC151248 (Accession XM_087143). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151248. LOC153222 (Accession XM_087631) is another VGAM1125 host target gene. LOC153222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153222 BINDING SITE, designated SEQ ID:39367, to the nucleotide sequence of VGAM1125 RNA, herein designated VGAM RNA, also designated SEQ ID:3836.

[40604] Another function of VGAM1125 is therefore inhibition of

LOC153222 (Accession XM_087631). Accordingly, utilities of VGAM1125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153222. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1126 (VGAM1126) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40605] VGAM1126 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1126 was detected is described hereinabove with reference to Figs. 1-8.

[40606] VGAM1126 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ononis Yellow Mosaic Virus. VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40607] VGAM1126 gene encodes a VGAM1126 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1126 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1126 precursor RNA is designated SEQ ID:1112, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1112 is located at position 5517 relative to the genome of Ononis Yellow Mosaic Virus.

[40608] VGAM1126 precursor RNA folds onto itself, forming VGAM1126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40609] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1126 folded precursor RNA into VGAM1126 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM1126 RNA is designated SEQ ID:3837, and is provided hereinbelow with reference to the sequence listing part.

[40610] VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1126 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40611] VGAM1126 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1126 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1126 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[40612] The complementary binding of VGAM1126 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1126 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1126 host target RNA into VGAM1126 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40613] It is appreciated that VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1126 host target genes. The mRNA of each one of this plurality of VGAM1126 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1126 RNA, herein designated VGAM RNA, and which when bound by VGAM1126 RNA causes inhibition of translation of respective one or more VGAM1126 host target proteins.

[40614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1126 gene, herein designated VGAM GENE, on one or more VGAM1126 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40615] It is yet further appreciated that a function of VGAM1126

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of viral infection by Ononis Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1126 correlate with, and may be deduced from, the identity of the host target genes which VGAM1126 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40616] Nucleotide sequences of the VGAM1126 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1126 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1126 are further described hereinbelow with reference to Table 1.

[40617] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1126 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1126 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40618] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1126 gene, herein designated VGAM is inhibition of expression of VGAM1126 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1126 correlate with, and may be deduced from, the identity of the target genes which VGAM1126 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40619] Adenylate Kinase 1 (AK1, Accession NM_000476) is a VGAM1126 host target gene. AK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK1 BINDING SITE, designated SEQ ID:6086, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40620] A function of VGAM1126 is therefore inhibition of Adenylate Kinase 1 (AK1, Accession NM_000476). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK1. Alkaline Phosphatase, Intestinal (ALPI, Accession

NM_001631) is another VGAM1126 host target gene. ALPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALPI BINDING SITE, designated SEQ ID:7342, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40621] Another function of VGAM1126 is therefore inhibition of Alkaline Phosphatase, Intestinal (ALPI, Accession NM_001631), a gene which is a glycoprotein phosphatase. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALPI. The function of ALPI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282) is another VGAM1126 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ ID:6950, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40622] Another function of VGAM1126 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 has been established by previous studies. The beta adaptin subunit of the clathrin coat assembly complex, also referred to as AP2-beta, was cloned from human, rat and bovine cDNA libraries by Ponnambalam et al. (1990) who found that the predicted 937-amino acid proteins are totally conserved between species. The protein is part of the AP2 coat assembly protein complex (see OMIM Ref. No. 601024) and links clathrin (OMIM Ref. No. 118960) to receptors in the coated vesicles. Druck et al. (1995) used a probe from the 3-prime UTR of the human cDNA to map the gene to chromosome 17. Hybrids with portions of chromosome 17

were then used to localize CLAPB1 to 17q11.2–q12.

[40623] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40624] Druck, T.; Gu, Y.; Prabhala. G.; Cannizzaro, L. A.; Park, S.–H.; Huebner, K.; Keen, J. H. : Chromosome localization of human genes for clathrin adaptor polypeptides AP2–beta and AP50 and the clathrin–binding protein, VCP. Genomics 30: 94–97, 1995. ; and

[40625] Ponnambalam, S.; Robinson, M. S.; Jackson, A. P.; Peiperl, L.; Parham, P. : Conservation and diversity in families of coated vesicle adaptins. J. Biol. Chem. 265: 4814–4820, 1990.

[40626] Further studies establishing the function and utilities of AP2B1 are found in John Hopkins OMIM database record ID 601025, and in cited publications numbered 9964–9965 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Aminophospholipid Transporter–like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916) is another VGAM1126 host target gene. ATP8A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP8A2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8A2 BINDING SITE, designated SEQ ID:44917, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40627] Another function of VGAM1126 is therefore inhibition of ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8A2. AXL Receptor Tyrosine Kinase (AXL, Accession NM_021913) is another VGAM1126 host target gene. AXL BINDING SITE1 and AXL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AXL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXL BINDING SITE1 and AXL BINDING SITE2, designated SEQ ID:22441 and SEQ ID:7420 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40628] Another function of VGAM1126 is therefore inhibition of AXL Receptor Tyrosine Kinase (AXL, Accession NM_021913). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXL. Bone Morphogenetic Protein 3 (osteogenic) (BMP3, Accession NM_001201) is another VGAM1126 host target gene. BMP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP3 BINDING SITE, designated SEQ ID:6865, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40629] Another function of VGAM1126 is therefore inhibition of Bone Morphogenetic Protein 3 (osteogenic) (BMP3, Accession NM_001201), a gene which induces cartilage and bone formation. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP3. The function of BMP3 has been established by previous studies. Dickinson et al. (1990) showed that in the mouse the Bmp-3 gene is

located on chromosome 5. Arguing from homology of synteny, they suggested that the cognate gene in man is located on either chromosome 4 or chromosome 7. Indeed, using cDNA probes for the analysis of somatic cell hybrid lines, Tabas et al. (1991) assigned the BMP3 gene to 4p14–q21. BMP2A (OMIM Ref. No. 112261) and BMP3 are members of the transforming growth factor–beta supergene family; BMP1 (OMIM Ref. No. 112264) is a novel regulatory protein.

[40630] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40631] Dickinson, M. E.; Kobrin, M. S.; Silan, C. M.; Kingsley, D. M.; Justice, M. J.; Miller, D. A.; Ceci, J. D.; Lock, L. F.; Lee, A.; Buchberg, A. M.; Siracusa, L. D.; Lyons, K. M.; Derynck, R.; Hogan, B. L. M.; Copeland, N. G.; Jenkins, N. A. : Chromosomal localization of seven members of the murine TGF–beta superfamily suggests close linkage to several morphogenetic mutant loci. *Genomics* 6: 505–520, 1990. ; and

[40632] Tabas, J. A.; Zasloff, M.; Wasmuth, J. J.; Emanuel, B. S.; Altherr, M. R.; McPherson, J. D.; Wozney, J. M.; Kaplan, F. S. : Bone morphogenetic protein: chromosomal localization of

human.

[40633] Further studies establishing the function and utilities of BMP3 are found in John Hopkins OMIM database record ID 112263, and in cited publications numbered 271 and 11629 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Corticotropin Releasing Hormone Receptor 1 (CRHR1, Accession NM_004382) is another VGAM1126 host target gene. CRHR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRHR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRHR1 BINDING SITE, designated SEQ ID:10606, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40634] Another function of VGAM1126 is therefore inhibition of Corticotropin Releasing Hormone Receptor 1 (CRHR1, Accession NM_004382), a gene which likely mediates physiological and behavioral response to stress. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CRHR1. The function of CRHR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM435. Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502) is another VGAM1126 host target gene. CX3CR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CX3CR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CX3CR1 BINDING SITE, designated SEQ ID:34975, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40635] Another function of VGAM1126 is therefore inhibition of Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502), a gene which mediates both the adhesive and migratory functions of fractalkine. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CX3CR1. The function of CX3CR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM25.Disabled Homolog 2, Mitogen-responsive Phosphoprotein (Drosophila) (DAB2, Accession NM_001343) is another VGAM1126 host target gene.

DAB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAB2 BINDING SITE, designated SEQ ID:7022, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40636] Another function of VGAM1126 is therefore inhibition of Disabled Homolog 2, Mitogen-responsive Phosphoprotein (Drosophila) (DAB2, Accession NM_001343), a gene which may be a component of the csf-1 signal transduction pathway. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAB2. The function of DAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM659.EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883) is another VGAM1126 host target gene.

EGFL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30960, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40637] Another function of VGAM1126 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL4. F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM_012308) is another VGAM1126 host target gene. FBXL11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL11 BINDING SITE, designated SEQ ID:14679, to the nucleotide sequence of VGAM1126 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3837.

[40638] Another function of VGAM1126 is therefore inhibition of F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM_012308), a gene which are BTB/POZ domain-containing zinc finger proteins implicated in oncogenesis. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL11. The function of FBXL11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404. Flotillin 2 (FLOT2, Accession NM_004475) is another VGAM1126 host target gene. FLOT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLOT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLOT2 BINDING SITE, designated SEQ ID:10792, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40639] Another function of VGAM1126 is therefore inhibition of Flotillin 2 (FLOT2, Accession NM_004475), a gene which

Epidermal surface antigen (flotillin 2). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLOT2. The function of FLOT2 has been established by previous studies. Human epidermal surface antigen-1 was identified as a 35-kD antigen by means of a mouse monoclonal antibody raised against human keratinocytes. The monoclonal antibody was found to cause keratinocyte dissociation in vitro; hence, the conclusion that the native protein is involved in cell adhesion. Cho et al. (1995) found that mouse Esa cDNA encodes a 379-amino acid protein that is 99.2% identical to the human, differing at only 3 amino acids. Cho et al. (1995) found that both 'nude' and control mice have a second Esa mRNA transcript that conserves amino acid sequence and molecular mass. The mouse and human 5-prime- and 3-prime untranslated sequences are conserved. Similar RNA folding patterns of the 5-prime untranslated region are predicted despite a 91-bp insertion in the mouse. Bickel et al. (1997) found that mouse Flot2 consistently copurifies with Flot1 (OMIM Ref. No. 606998) and with caveolin-1 (OMIM Ref. No. 601047) in the purification of caveolin-rich membranes. Baumann et al. (2000) screened a yeast

2-hybrid library using the N-terminal region of CAP (OMIM Ref. No. 605264) and identified the caveolar protein flotillin. Flotillin forms a ternary complex with CAP and the CBL protooncogene product (OMIM Ref. No. 165360), directing the localization of the CAP-CBL complex to a lipid raft subdomain of the plasma membrane. Localization of the CBL-CAP complex to lipid rafts generates a pathway that is crucial in the regulation of glucose uptake. Schroeder et al. (1991) isolated a cDNA for an epidermal surface antigen believed to be involved in epidermal cell adhesion. By analysis of a somatic cell hybrid panel and in situ hybridization using the ESA cDNA, the gene was mapped to 17q11-q12 in the region containing the NF1 gene (OMIM Ref. No. 162200). Using a RFLP within the ESA1 gene, they showed tight linkage of ESA1 with NF1; maximal lod = 6.92 at theta = 0.0. By studying somatic cell hybrids carrying the 2 chromosome 17 translocations with breakpoints within the NF1 gene, t(1;17) and t(17;22), Schroeder et al. (1991) showed that the ESA1 gene is located centromeric to the t(1;17) breakpoint. It remained to be determined whether this represented another of the genes located within the NF1 gene and transcribed in the opposite direction. Kayes et al.

(1992) made that determination; physical mapping of an M17S1 cDNA on somatic cell hybrids, yeast artificial chromosomes, and DNA from an NF1 patient with a deletion involving an entire NF1 allele showed that M17S1 is located at least 180 kb centromeric to the NF1 gene. The distance between the genes suggested that M17S1 is unlikely to contribute to the NF1 phenotype. Cho et al.

(1995) mapped the mouse Esa gene to chromosome 11. Although the mouse Esa gene and the 'nude' locus map to the same region of chromosome 11, Cho et al. (1995) detected no abnormalities in protein, mRNA, cDNA or genomic Esa sequences in nude mice.

[40640] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40641] Cho, Y.-J.; Chema, D.; Moskow, J. J.; Cho, M.; Schroeder, W. T.; Overbeek, P.; Buchberg, A. M.; Duvic, M. : Epidermal surface antigen (MS17S1) is highly conserved between mouse and human. Genomics 27: 251-258, 1995. ; and

[40642] Schroeder, W. T.; Siciliano, M. J.; Stewart-Galetka, S. L.; Duvic, M. : The human gene for an epidermal surface antigen (M17S1) is located at 17q11-12. Genomics 11: 481-482, 1991.

[40643] Further studies establishing the function and utilities of FLOT2 are found in John Hopkins OMIM database record ID 131560, and in cited publications numbered 4598–4603 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FXYD Domain Containing Ion Transport Regulator 6 (FXYD6, Accession NM_022003) is another VGAM1126 host target gene. FXYD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FXYD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FXYD6 BINDING SITE, designated SEQ ID:22546, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40644] Another function of VGAM1126 is therefore inhibition of FXYD Domain Containing Ion Transport Regulator 6 (FXYD6, Accession NM_022003). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FXYD6. Growth Factor Independent 1 (GFI1, Accession NM_005263) is another VGAM1126 host target gene. GFI1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFI1 BINDING SITE, designated SEQ ID:11768, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40645] Another function of VGAM1126 is therefore inhibition of Growth Factor Independent 1 (GFI1, Accession NM_005263). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFI1. Insulin-like Growth Factor 2 (somatomedin A) (IGF2, Accession NM_000612) is another VGAM1126 host target gene. IGF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2 BINDING SITE, designated SEQ ID:6214, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40646] Another function of VGAM1126 is therefore inhibition of Insulin-like Growth Factor 2 (somatomedin A) (IGF2, Accession NM_000612). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2. Inositol Polyphosphate-1-phosphatase (INPP1, Accession NM_002194) is another VGAM1126 host target gene. INPP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by INPP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP1 BINDING SITE, designated SEQ ID:7950, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40647] Another function of VGAM1126 is therefore inhibition of Inositol Polyphosphate-1-phosphatase (INPP1, Accession NM_002194), a gene which hydrolyzes inositol 1,3,4-trisphosphate to inositol 1,4-bisphosphate. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP1. The function of INPP1 has been established by previous studies. Cells respond to extracellu-

lar stimuli through complicated networks. Phosphatidylinositol turnover plays a key role in intracellular signaling. Inositol polyphosphate 1-phosphatase, an enzyme in the phosphatidylinositol signaling pathway, catalyzes the hydrolysis of the 1 position phosphate from inositol 1,3,4-trisphosphate (Ins(1,3,4)P₃) and inositol 1,4-bisphosphate (Ins(1,4)P₂). York et al. (1993) isolated a cDNA for the human counterpart by low stringency hybridization using a cDNA encoding the bovine enzyme. The 1.74-kb human cDNA predicted a protein of 399 amino acids. The human and bovine enzymes show 84% amino acid sequence identity. Northern blot analysis of a variety of human tissues demonstrated that a 1.9-kb mRNA is ubiquitously expressed, with highest levels in pancreas and kidney. York et al. (1993) suggested INPP1 as a candidate gene for inherited psychiatric disorders that respond to lithium ions, an inhibitor of the enzyme. Woodcock et al. (2002) studied the role of inositol polyphosphates in cardiac hypertrophy, using primary cultures of neonatal rat ventricular cardiomyocytes as a model. Hypertrophy was induced by stimulating alpha-adrenergic receptors (see OMIM Ref. No. ADRA1B; 104220) or by the spontaneous contraction of dense cul-

tures. Both hypertrophy models showed increased levels of Ins(1,4)P₂ as well as the characteristic increased expression of several marker genes and increased ribosome synthesis. Transfection and overexpression of INPP1 reduced expression of hypertrophy markers and reduced the increase in ribosomal DNA transcription. Ins(1,4)P₂ levels were also increased in mouse hearts hypertrophied by pressure overload. Woodcock et al. (2002) concluded that reduced INPP1 activity may have a role in cardiac hypertrophy.

[40648] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40649] Okabe, I.; Nussbaum, R. L. : Identification and chromosomal mapping of the mouse inositol polyphosphate 1-phosphatase gene. *Genomics* 30: 358–360, 1995. ; and

[40650] Woodcock, E. A.; Wang, B. H.; Arthur, J. F.; Lennard, A.; Matkovich, S. J.; Du, X.-J.; Brown, J. H.; Hannan, R. D. : Inositol polyphosphate 1-phosphatase is a novel antihypertrophic factor.

[40651] Further studies establishing the function and utilities of INPP1 are found in John Hopkins OMIM database record ID 147263, and in cited publications numbered 4970–4972

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. L1 Cell Adhesion Molecule (hydrocephalus, stenosis of aqueduct of Sylvius 1, MASA (mental retardation, aphasia, shuffling gait and adducted thumbs) Syndrome, Spastic Paraplegia 1) (L1CAM, Accession NM_024003) is another VGAM1126 host target gene. L1CAM BINDING SITE1 and L1CAM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by L1CAM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L1CAM BINDING SITE1 and L1CAM BINDING SITE2, designated SEQ ID:23430 and SEQ ID:6002 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40652] Another function of VGAM1126 is therefore inhibition of L1 Cell Adhesion Molecule (hydrocephalus, stenosis of aqueduct of Sylvius 1, MASA (mental retardation, aphasia, shuffling gait and adducted thumbs) Syndrome, Spastic Paraplegia 1) (L1CAM, Accession NM_024003). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with L1CAM. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507) is another VGAM1126 host target gene. NGFR BINDING SITE1 and NGFR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NGFR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE1 and NGFR BINDING SITE2, designated SEQ ID:8330 and SEQ ID:8331 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40653] Another function of VGAM1126 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM212. Neurexin 1 (NRXN1, Accession NM_004801) is another VGAM1126 host target

gene. NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2, designated SEQ ID:11222 and SEQ ID:26788 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40654] Another function of VGAM1126 is therefore inhibition of Neurexin 1 (NRXN1, Accession NM_004801), a gene which may be involved in cell recognition, cell adhesion, and mediate intracellular signaling. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN1. The function of NRXN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Protocadherin 11 Y-linked (PCDH11Y, Accession NM_032973) is another VGAM1126 host target gene. PCDH11Y BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PCDH11Y, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11Y BINDING SITE, designated SEQ ID:26822, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40655] Another function of VGAM1126 is therefore inhibition of Protocadherin 11 Y-linked (PCDH11Y, Accession NM_032973). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11Y. PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746) is another VGAM1126 host target gene. PCTK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCTK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTK3 BINDING SITE, designated SEQ ID:36126, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40656] Another function of VGAM1126 is therefore inhibition of

PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746), a gene which may play a role in signal transduction cascades in terminally differentiated cells. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCTK3. The function of PCTK3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132. Protein Phosphatase 2, Regulatory Subunit B (B56), Beta Isoform (PPP2R5B, Accession NM_006244) is another VGAM1126 host target gene. PPP2R5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5B BINDING SITE, designated SEQ ID:12913, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40657] Another function of VGAM1126 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Beta Isoform (PPP2R5B, Accession NM_006244), a gene which

is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5B. The function of PPP2R5B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM264. Pleckstrin Homology, Sec7 and Coiled/coil Domains 4 (PSCD4, Accession NM_013385) is another VGAM1126 host target gene. PSCD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSCD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSCD4 BINDING SITE, designated SEQ ID:15036, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40658] Another function of VGAM1126 is therefore inhibition of Pleckstrin Homology, Sec7 and Coiled/coil Domains 4 (PSCD4, Accession NM_013385), a gene which promotes guanine-nucleotide exchange on arf1 and arf5. Accordingly, utilities of VGAM1126 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with PSCD4. The function of PSCD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to

VGAM615. Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM_046472) is another VGAM1126 host target gene. PYCR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYCR1 BINDING SITE, designated SEQ ID:34728, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40659] Another function of VGAM1126 is therefore inhibition of Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM_046472), a gene which catalyzes the NAD(P)H-dependent conversion of pyrroline-5-carboxylate to proline. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYCR1.

The function of PYCR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Solute Carrier Family 2 (facilitated glucose transporter), Member 3 (SLC2A3, Accession NM_006931) is another VGAM1126 host target gene. SLC2A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A3 BINDING SITE, designated SEQ ID:13816, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40660] Another function of VGAM1126 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 3 (SLC2A3, Accession NM_006931), a gene which probably is a neuronal glucose transporter. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A3. The function of SLC2A3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM247.SNL (Accession NM_003088) is another VGAM1126 host target gene. SNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNL BINDING SITE, designated SEQ ID:9059, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40661] Another function of VGAM1126 is therefore inhibition of SNL (Accession NM_003088), a gene which organizes filamentous actin into bundles with a minimum of 4.1:1 actin/fascin ratio. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNL. The function of SNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM675.Transforming Growth Factor, Beta 3 (TGFB3, Accession NM_003239) is another VGAM1126 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

TGFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB3 BINDING SITE, designated SEQ ID:9233, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40662] Another function of VGAM1126 is therefore inhibition of Transforming Growth Factor, Beta 3 (TGFB3, Accession NM_003239), a gene which is involved in embryogenesis and cell differentiation. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB3. The function of TGFB3 has been established by previous studies. Type beta transforming growth factors are polypeptides that act hormonally to control the proliferation and differentiation of multiple cell types. A cDNA clone for a third form of TGFB was isolated by ten Dijke et al. (1988). The C-terminal 112 amino acids of TGF-beta-3 share approximately 80% sequence identity with beta-1 (OMIM Ref. No. 190180) and beta-2 (OMIM Ref. No. 190220). By Southern analysis of DNA prepared from somatic cell hybrids and by in situ hybridization, ten Dijke et

al. (1988) assigned the TGFB3 gene to 14q23–q24. Barton et al. (1988) likewise assigned the TGFB3 gene to chromosome 14 and regionalized it to 14q24 by Southern blot analysis of hybrid cell DNAs and by in situ hybridization. The homologous gene in the mouse, Tsfb–3, was mapped to chromosome 12 (Barton et al., 1988; Dickinson et al., 1990). Graycar et al. (1989) purified to apparent homogeneity human TGFB3 and evaluated its activities in comparison to TGFB1 and TGFB2. Lee and Nowak (2001) compared expression of the TGFB isoforms in normal myometrium and benign leiomyoma tumors of the uterus (OMIM Ref. No. 150699) and examined the effects of TGFBs on cell proliferation and collagen production by these cells in vitro. Northern blot analysis showed that the levels of TGFB1 mRNA were similar between leiomyoma and myometrium, whereas leiomyoma showed 5-fold higher levels of expression of TGFB3 mRNA than autologous myometrium. Expression of TGFB3 protein detected by immunohistochemistry was much more intense in leiomyoma tissues than in corresponding myometrium. The authors concluded that their results support the hypothesis that alterations in the TGFB system produce loss of sensitivity to the antiproliferative effects of TGFB, and

increased expression of TGFB3 may contribute to the growth of these tumors. Animal model experiments lend further support to the function of TGFB3. Proetzel et al. (1995) produced Tgfb3-null mice in which exon 6 of the Tgfb3 gene was replaced by the neomycin-resistance gene. Whereas heterozygotes had no apparent phenotypic change, homozygotes had an incompletely penetrant failure of the palatal shelves to fuse, leading to cleft palate. The defect appeared to result from impaired adhesion of the apposing medial edge epithelial of the palatal shelves and subsequent elimination of the midline epithelial seam. No craniofacial abnormalities were observed. Defective palatogenesis was also found in homozygous Tgfb3-null mutant mice by Kaartinen et al. (1995) who also found a consistent delay in pulmonary development. They suggested that the study demonstrates an essential function for TGF-beta-3 in normal palate and lung morphogenesis and implicates this cytokine in epithelial-mesenchymal interaction.

[40663] It is appreciated that the abovementioned animal model for TGFB3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[40664] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40665] Graycar, J. L.; Miller, D. A.; Arrick, B. A.; Lyons, R. M.; Moses, H. L.; Derynck, R. : Human transforming growth factor-beta-3: recombinant expression, purification, and biological activities in comparison with transforming growth factors-beta-1 and beta-2. *Molec. Endocr.* 3: 1977-1986, 1989. ; and

[40666] Proetzel, G.; Pawlowski, S. A.; Wiles, M. V.; Yin, M.; Boivin, G. P.; Howles, P. N.; Ding, J.; Ferguson, M. W. J.; Doetschman, T. : Transforming growth factor-beta-3 is required for seco.

[40667] Further studies establishing the function and utilities of TGFB3 are found in John Hopkins OMIM database record ID 190230, and in cited publications numbered 1235 and 5953-5959 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Toll-like Receptor 5 (TLR5, Accession NM_003268) is another VGAM1126 host target gene. TLR5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLR5 BINDING SITE, designated SEQ ID:9276, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40668] Another function of VGAM1126 is therefore inhibition of Toll-like Receptor 5 (TLR5, Accession NM_003268), a gene which participates in the innate immune response to bacterial flagellins. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLR5. The function of TLR5 has been established by previous studies. By searching an EST database for human Toll homologs, Chaudhary et al. (1998) identified cDNA sequences from 2 genes that they called TIL3 and TIL4 (TLR2; 603028). Muzio et al. (2000) determined the differential expression pattern of the TLRs in leukocytes. Like TLR2 and TLR4, TLR5 was expressed in myelomonocytic cells, but at lower levels. Hayashi et al. (2001) showed that expression of TLR5 induces NF-kappa-B activation and TNFA (OMIM Ref. No. 191160) production. Pathogen-associated molecular patterns (PAMPs) known to stimulate other TLR family members failed to stimulate TLR5; however, luciferase reporter

assays indicated TLR5 activation in gram-positive and -negative bacterial culture supernatants. By fractionation of *Listeria* culture supernatants followed by SDS-PAGE, Hayashi et al. (2001) identified flagellin as the TLR5 ligand. Flagellin, a principal component of bacterial flagella, is a virulence factor recognized by the innate immune system in plants, insects, and mammals. Expression of flagellin in nonflagellated bacteria resulted in TLR5 activation, and deletion of flagellin from flagellated bacteria abrogated TLR5 activation. Hayashi et al. (2001) demonstrated that injection of flagellin induces the production of IL6 (OMIM Ref. No. 147620) in wildtype mice, but not in those lacking the MyD88 (OMIM Ref. No. 602170) adaptor protein, required for TLR signaling. Hayashi et al. (2001) concluded that TLR5 is a pattern-recognition receptor and that its PAMP is flagellin, a protein with conserved N and C termini in a broad group of motile pathogens.

[40669] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40670] Chaudhary, P. M.; Ferguson, C.; Nguyen, V.; Nguyen, O.; Massa, H. F.; Eby, M.; Jasmin, A.; Trask, B. J.; Hood, L.; Nelson, P. S. : Cloning and characterization of two Toll/

interleukin-1 receptor-like genes TIL3 and TIL4: evidence for a multi-gene receptor family in humans. Blood 91: 4020-4027, 1998. ; and

[40671] Hayashi, F.; Smith, K. D.; Ozinsky, A.; Hawn, T. R.; Yi, E. C.; Goodlett, D. R.; Eng, J. K.; Akira, S.; Underhill, D. M.; Aderem, A. : The innate immune response to bacterial flagellin.

[40672] Further studies establishing the function and utilities of TLR5 are found in John Hopkins OMIM database record ID 603031, and in cited publications numbered 7953, 673 and 9837-9838 listed in the bibliography section herein-below, which are also hereby incorporated by reference. Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788) is another VGAM1126 host target gene. UBE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4A BINDING SITE, designated SEQ ID:11195, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40673] Another function of VGAM1126 is therefore inhibition of Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788), a gene which binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE4A. The function of UBE4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60. ABLIM (Accession NM_002313) is another VGAM1126 host target gene. ABLIM BINDING SITE1 and ABLIM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABLIM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABLIM BINDING SITE1 and ABLIM BINDING SITE2, designated SEQ ID:8110 and SEQ ID:13543 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40674] Another function of VGAM1126 is therefore inhibition of

ABLIM (Accession NM_002313). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABLIM. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM1126 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25512, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40675] Another function of VGAM1126 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289) is another VGAM1126 host target gene. CLIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of CLIC2 BINDING SITE, designated SEQ ID:6966, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40676] Another function of VGAM1126 is therefore inhibition of Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC2. Calsyntenin 2 (CLSTN2, Accession NM_022131) is another VGAM1126 host target gene. CLSTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLSTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN2 BINDING SITE, designated SEQ ID:22695, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40677] Another function of VGAM1126 is therefore inhibition of Calsyntenin 2 (CLSTN2, Accession NM_022131). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with CLSTN2. D15Wsu75e (Accession XM_039495) is another VGAM1126 host target gene. D15Wsu75e BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D15Wsu75e, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D15Wsu75e BINDING SITE, designated SEQ ID:33100, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40678] Another function of VGAM1126 is therefore inhibition of D15Wsu75e (Accession XM_039495). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D15Wsu75e. DKFZP564L2423 (Accession XM_031015) is another VGAM1126 host target gene. DKFZP564L2423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564L2423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564L2423 BINDING SITE, designated SEQ ID:31258, to the nucleotide sequence of

VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40679] Another function of VGAM1126 is therefore inhibition of DKFZP564L2423 (Accession XM_031015). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564L2423. DKFZp761G0313 (Accession XM_038026) is another VGAM1126 host target gene. DKFZp761G0313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761G0313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761G0313 BINDING SITE, designated SEQ ID:32739, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40680] Another function of VGAM1126 is therefore inhibition of DKFZp761G0313 (Accession XM_038026). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761G0313. Fer-1-like 4 (C. elegans) (FER1L4, Accession NM_025206) is another VGAM1126 host target

gene. FER1L4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FER1L4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FER1L4 BINDING SITE, designated SEQ ID:24872, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40681] Another function of VGAM1126 is therefore inhibition of Fer-1-like 4 (*C. elegans*) (FER1L4, Accession NM_025206). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FER1L4. FLJ11000 (Accession NM_018295) is another VGAM1126 host target gene. FLJ11000 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11000 BINDING SITE, designated SEQ ID:20284, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ

ID:3837.

[40682] Another function of VGAM1126 is therefore inhibition of FLJ11000 (Accession NM_018295). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11000. FLJ12294 (Accession NM_025100) is another VGAM1126 host target gene. FLJ12294 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12294 BINDING SITE, designated SEQ ID:24742, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40683] Another function of VGAM1126 is therefore inhibition of FLJ12294 (Accession NM_025100). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12294. FLJ12595 (Accession NM_024994) is another VGAM1126 host target gene. FLJ12595 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12595, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12595 BINDING SITE, designated SEQ ID:24557, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40684] Another function of VGAM1126 is therefore inhibition of FLJ12595 (Accession NM_024994). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12595. FLJ13204 (Accession NM_024761) is another VGAM1126 host target gene. FLJ13204 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13204 BINDING SITE, designated SEQ ID:24113, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40685] Another function of VGAM1126 is therefore inhibition of FLJ13204 (Accession NM_024761). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13204. FLJ13391 (Accession NM_032181) is another VGAM1126 host target gene. FLJ13391 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13391 BINDING SITE, designated SEQ ID:25894, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40686] Another function of VGAM1126 is therefore inhibition of FLJ13391 (Accession NM_032181). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13391. FLJ13881 (Accession NM_024729) is another VGAM1126 host target gene. FLJ13881 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13881 BINDING SITE, designated SEQ ID:24065, to the nucleotide

sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40687] Another function of VGAM1126 is therefore inhibition of FLJ13881 (Accession NM_024729). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13881. FLJ20128 (Accession NM_017679) is another VGAM1126 host target gene. FLJ20128 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20128 BINDING SITE, designated SEQ ID:19222, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40688] Another function of VGAM1126 is therefore inhibition of FLJ20128 (Accession NM_017679). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20128. FLJ20489 (Accession NM_017842) is another VGAM1126 host target gene. FLJ20489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ20489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20489 BINDING SITE, designated SEQ ID:19506, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40689] Another function of VGAM1126 is therefore inhibition of FLJ20489 (Accession NM_017842). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20489. FLJ22169 (Accession NM_024085) is another VGAM1126 host target gene. FLJ22169 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22169 BINDING SITE, designated SEQ ID:23520, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40690] Another function of VGAM1126 is therefore inhibition of FLJ22169 (Accession NM_024085). Accordingly, utilities of

VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22169. FLJ30663 (Accession XM_086046) is another VGAM1126 host target gene. FLJ30663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30663 BINDING SITE, designated SEQ ID:38461, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40691] Another function of VGAM1126 is therefore inhibition of FLJ30663 (Accession XM_086046). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30663. Glycoprotein V (platelet) (GP5, Accession NM_004488) is another VGAM1126 host target gene. GP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

GP5 BINDING SITE, designated SEQ ID:10816, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40692] Another function of VGAM1126 is therefore inhibition of Glycoprotein V (platelet) (GP5, Accession NM_004488). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GP5. HCCA2 (Accession XM_039894) is another VGAM1126 host target gene. HCCA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HCCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCCA2 BINDING SITE, designated SEQ ID:33202, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40693] Another function of VGAM1126 is therefore inhibition of HCCA2 (Accession XM_039894). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCCA2. KIAA0237 (Accession NM_014747) is another VGAM1126 host target gene. KIAA0237 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16439, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40694] Another function of VGAM1126 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0285 (Accession NM_014807) is another VGAM1126 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16749, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40695] Another function of VGAM1126 is therefore inhibition of

KIAA0285 (Accession NM_014807). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. KIAA0397 (Accession XM_029438) is another VGAM1126 host target gene. KIAA0397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0397 BINDING SITE, designated SEQ ID:30894, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40696] Another function of VGAM1126 is therefore inhibition of KIAA0397 (Accession XM_029438). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0397. KIAA0427 (Accession NM_014772) is another VGAM1126 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16572, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40697] Another function of VGAM1126 is therefore inhibition of KIAA0427 (Accession NM_014772). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. KIAA0471 (Accession NM_014857) is another VGAM1126 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16908, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40698] Another function of VGAM1126 is therefore inhibition of KIAA0471 (Accession NM_014857). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. KIAA0481 (Accession XM_050144) is another

VGAM1126 host target gene. KIAA0481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0481 BINDING SITE, designated SEQ ID:35567, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40699] Another function of VGAM1126 is therefore inhibition of KIAA0481 (Accession XM_050144). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0481. KIAA0563 (Accession NM_014834) is another VGAM1126 host target gene. KIAA0563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0563 BINDING SITE, designated SEQ ID:16839, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40700] Another function of VGAM1126 is therefore inhibition of KIAA0563 (Accession NM_014834). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0563. KIAA0978 (Accession XM_047013) is another VGAM1126 host target gene. KIAA0978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0978, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0978 BINDING SITE, designated SEQ ID:34886, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40701] Another function of VGAM1126 is therefore inhibition of KIAA0978 (Accession XM_047013). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0978. KIAA1465 (Accession XM_027396) is another VGAM1126 host target gene. KIAA1465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1465, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1465 BINDING SITE, designated SEQ ID:30500, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40702] Another function of VGAM1126 is therefore inhibition of KIAA1465 (Accession XM_027396). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1465. KIAA1554 (Accession XM_170834) is another VGAM1126 host target gene. KIAA1554 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1554, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1554 BINDING SITE, designated SEQ ID:45608, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40703] Another function of VGAM1126 is therefore inhibition of KIAA1554 (Accession XM_170834). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1554. KIAA1727 (Accession XM_034262) is another VGAM1126 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32032, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40704] Another function of VGAM1126 is therefore inhibition of KIAA1727 (Accession XM_034262). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. KIAA1909 (Accession XM_057996) is another VGAM1126 host target gene. KIAA1909 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1909 BINDING SITE, designated SEQ ID:36557, to the nucleotide sequence of VGAM1126 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3837.

[40705] Another function of VGAM1126 is therefore inhibition of KIAA1909 (Accession XM_057996). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1909. KIAA1944 (Accession XM_062545) is another VGAM1126 host target gene. KIAA1944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1944 BINDING SITE, designated SEQ ID:37226, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40706] Another function of VGAM1126 is therefore inhibition of KIAA1944 (Accession XM_062545). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1944. MGC1136 (Accession NM_024025) is another VGAM1126 host target gene. MGC1136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC1136, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1136 BINDING SITE, designated SEQ ID:23452, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40707] Another function of VGAM1126 is therefore inhibition of MGC1136 (Accession NM_024025). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1136. MGC13170 (Accession NM_032712) is another VGAM1126 host target gene. MGC13170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13170 BINDING SITE, designated SEQ ID:26430, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40708] Another function of VGAM1126 is therefore inhibition of MGC13170 (Accession NM_032712). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC13170. MGC17998 (Accession NM_144997) is another VGAM1126 host target gene. MGC17998 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC17998, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC17998 BINDING SITE, designated SEQ ID:29602, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40709] Another function of VGAM1126 is therefore inhibition of MGC17998 (Accession NM_144997). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC17998. Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971) is another VGAM1126 host target gene. MRPL20 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MRPL20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL20 BINDING SITE,

designated SEQ ID:19695, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40710] Another function of VGAM1126 is therefore inhibition of Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL20. Opiate Receptor-like 1 (OPRL1, Accession NM_000913) is another VGAM1126 host target gene. OPRL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPRL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPRL1 BINDING SITE, designated SEQ ID:6614, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40711] Another function of VGAM1126 is therefore inhibition of Opiate Receptor-like 1 (OPRL1, Accession NM_000913). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPRL1. PDZ Domain Containing 2

(PDZD2, Accession XM_087705) is another VGAM1126 host target gene. PDZD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PDZD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDZD2 BINDING SITE, designated SEQ ID:39389, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40712] Another function of VGAM1126 is therefore inhibition of PDZ Domain Containing 2 (PDZD2, Accession XM_087705). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDZD2. PME-1 (Accession NM_016147) is another VGAM1126 host target gene. PME-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PME-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PME-1 BINDING SITE, designated SEQ ID:18232, to the nucleotide sequence of VGAM1126 RNA,

herein designated VGAM RNA, also designated SEQ ID:3837.

[40713] Another function of VGAM1126 is therefore inhibition of PME-1 (Accession NM_016147). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PME-1. PRO0132 (Accession NM_014116) is another VGAM1126 host target gene. PRO0132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0132 BINDING SITE, designated SEQ ID:15368, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40714] Another function of VGAM1126 is therefore inhibition of PRO0132 (Accession NM_014116). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0132. Syndecan 3 (N-syndecan) (SDC3, Accession NM_014654) is another VGAM1126 host target gene. SDC3 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by SDC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC3 BINDING SITE, designated SEQ ID:16088, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40715] Another function of VGAM1126 is therefore inhibition of Syndecan 3 (N-syndecan) (SDC3, Accession NM_014654). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC3. SEP15 (Accession NM_004261) is another VGAM1126 host target gene. SEP15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEP15 BINDING SITE, designated SEQ ID:10453, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40716] Another function of VGAM1126 is therefore inhibition of

SEP15 (Accession NM_004261). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEP15. Sideroflexin 5 (SFXN5, Accession NM_144579) is another VGAM1126 host target gene. SFXN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFXN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFXN5 BINDING SITE, designated SEQ ID:29384, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40717] Another function of VGAM1126 is therefore inhibition of Sideroflexin 5 (SFXN5, Accession NM_144579). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFXN5. SKIP (Accession NM_130766) is another VGAM1126 host target gene. SKIP BINDING SITE1 and SKIP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SKIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of SKIP BINDING SITE1 and SKIP BINDING SITE2, designated SEQ ID:28260 and SEQ ID:18597 respectively, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40718] Another function of VGAM1126 is therefore inhibition of SKIP (Accession NM_130766). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIP. SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM_050403) is another VGAM1126 host target gene. SMC1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMC1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMC1L1 BINDING SITE, designated SEQ ID:35617, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40719] Another function of VGAM1126 is therefore inhibition of SMC1 Structural Maintenance of Chromosomes 1-like 1 (yeast) (SMC1L1, Accession XM_050403). Accordingly,

utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMC1L1. Smith–Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM_144774) is another VGAM1126 host target gene. SMCR5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMCR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMCR5 BINDING SITE, designated SEQ ID:29561, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40720] Another function of VGAM1126 is therefore inhibition of Smith–Magenis Syndrome Chromosome Region, Candidate 5 (SMCR5, Accession NM_144774). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMCR5. Syntaphilin (SNPH, Accession NM_014723) is another VGAM1126 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16289, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40721] Another function of VGAM1126 is therefore inhibition of Syntaphilin (SNPH, Accession NM_014723). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. Signal Transducer and Activator of Transcription 5A (STAT5A, Accession NM_003152) is another VGAM1126 host target gene. STAT5A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STAT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT5A BINDING SITE, designated SEQ ID:9126, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40722] Another function of VGAM1126 is therefore inhibition of Signal Transducer and Activator of Transcription 5A (STAT5A, Accession NM_003152). Accordingly, utilities of

VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT5A. Synaptotagmin XII (SYT12, Accession XM_170657) is another VGAM1126 host target gene. SYT12 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SYT12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT12 BINDING SITE, designated SEQ ID:45429, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40723] Another function of VGAM1126 is therefore inhibition of Synaptotagmin XII (SYT12, Accession XM_170657). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT12. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023) is another VGAM1126 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27572, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40724] Another function of VGAM1126 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. LOC116071 (Accession NM_138456) is another VGAM1126 host target gene. LOC116071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116071 BINDING SITE, designated SEQ ID:28815, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40725] Another function of VGAM1126 is therefore inhibition of LOC116071 (Accession NM_138456). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC116071. LOC118738 (Accession XM_061125) is another VGAM1126 host target gene. LOC118738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118738 BINDING SITE, designated SEQ ID:37194, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40726] Another function of VGAM1126 is therefore inhibition of LOC118738 (Accession XM_061125). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118738. LOC127702 (Accession XM_060619) is another VGAM1126 host target gene. LOC127702 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127702, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127702 BINDING SITE, designated SEQ ID:37179, to

the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40727] Another function of VGAM1126 is therefore inhibition of LOC127702 (Accession XM_060619). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127702. LOC130644 (Accession XM_065813) is another VGAM1126 host target gene. LOC130644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130644 BINDING SITE, designated SEQ ID:37304, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40728] Another function of VGAM1126 is therefore inhibition of LOC130644 (Accession XM_065813). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130644. LOC132166 (Accession XM_059574) is another VGAM1126 host target gene. LOC132166 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC132166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132166 BINDING SITE, designated SEQ ID:37020, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40729] Another function of VGAM1126 is therefore inhibition of LOC132166 (Accession XM_059574). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132166. LOC145761 (Accession XM_096855) is another VGAM1126 host target gene. LOC145761 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145761 BINDING SITE, designated SEQ ID:40582, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40730] Another function of VGAM1126 is therefore inhibition of LOC145761 (Accession XM_096855). Accordingly, utilities

of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145761. LOC145989 (Accession XM_004815) is another VGAM1126 host target gene. LOC145989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145989 BINDING SITE, designated SEQ ID:29947, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40731] Another function of VGAM1126 is therefore inhibition of LOC145989 (Accession XM_004815). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145989. LOC147071 (Accession XM_054031) is another VGAM1126 host target gene. LOC147071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC147071 BINDING SITE, designated SEQ ID:36132, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40732] Another function of VGAM1126 is therefore inhibition of LOC147071 (Accession XM_054031). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147071. LOC148894 (Accession XM_097542) is another VGAM1126 host target gene. LOC148894 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148894 BINDING SITE, designated SEQ ID:40917, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40733] Another function of VGAM1126 is therefore inhibition of LOC148894 (Accession XM_097542). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148894. LOC151068 (Accession XM_098000) is another VGAM1126 host target gene. LOC151068 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151068 BINDING SITE, designated SEQ ID:41296, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40734] Another function of VGAM1126 is therefore inhibition of LOC151068 (Accession XM_098000). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151068. LOC152286 (Accession XM_098188) is another VGAM1126 host target gene. LOC152286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152286 BINDING SITE, designated SEQ ID:41461, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40735] Another function of VGAM1126 is therefore inhibition of

LOC152286 (Accession XM_098188). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152286. LOC152915 (Accession XM_040172) is another VGAM1126 host target gene. LOC152915 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152915 BINDING SITE, designated SEQ ID:33268, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40736] Another function of VGAM1126 is therefore inhibition of LOC152915 (Accession XM_040172). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152915. LOC153338 (Accession XM_098361) is another VGAM1126 host target gene. LOC153338 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153338, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC153338 BINDING SITE, designated SEQ ID:41608, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40737] Another function of VGAM1126 is therefore inhibition of LOC153338 (Accession XM_098361). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153338. LOC158230 (Accession XM_088517) is another VGAM1126 host target gene. LOC158230 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158230 BINDING SITE, designated SEQ ID:39766, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40738] Another function of VGAM1126 is therefore inhibition of LOC158230 (Accession XM_088517). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158230. LOC158969 (Accession XM_088728) is an-

other VGAM1126 host target gene. LOC158969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158969 BINDING SITE, designated SEQ ID:39919, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40739] Another function of VGAM1126 is therefore inhibition of LOC158969 (Accession XM_088728). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158969. LOC200982 (Accession XM_117305) is another VGAM1126 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43372, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40740] Another function of VGAM1126 is therefore inhibition of LOC200982 (Accession XM_117305). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. LOC201173 (Accession XM_113312) is another VGAM1126 host target gene. LOC201173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201173 BINDING SITE, designated SEQ ID:42211, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40741] Another function of VGAM1126 is therefore inhibition of LOC201173 (Accession XM_113312). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201173. LOC201220 (Accession XM_113321) is another VGAM1126 host target gene. LOC201220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201220, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201220 BINDING SITE, designated SEQ ID:42219, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40742] Another function of VGAM1126 is therefore inhibition of LOC201220 (Accession XM_113321). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201220. LOC201229 (Accession XM_113925) is another VGAM1126 host target gene. LOC201229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201229 BINDING SITE, designated SEQ ID:42542, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40743] Another function of VGAM1126 is therefore inhibition of LOC201229 (Accession XM_113925). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC201229. LOC203197 (Accession XM_114645) is another VGAM1126 host target gene. LOC203197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203197 BINDING SITE, designated SEQ ID:43009, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40744] Another function of VGAM1126 is therefore inhibition of LOC203197 (Accession XM_114645). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203197. LOC205693 (Accession XM_120345) is another VGAM1126 host target gene. LOC205693 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205693 BINDING SITE, designated SEQ ID:43608, to the nucleotide sequence of VGAM1126 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3837.

[40745] Another function of VGAM1126 is therefore inhibition of LOC205693 (Accession XM_120345). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205693. LOC220766 (Accession XM_165471) is another VGAM1126 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43647, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40746] Another function of VGAM1126 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC221463 (Accession XM_166374) is another VGAM1126 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221463, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44200, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40747] Another function of VGAM1126 is therefore inhibition of LOC221463 (Accession XM_166374). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221463. LOC223073 (Accession XM_170293) is another VGAM1126 host target gene. LOC223073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC223073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC223073 BINDING SITE, designated SEQ ID:45316, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40748] Another function of VGAM1126 is therefore inhibition of LOC223073 (Accession XM_170293). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC223073. LOC257054 (Accession XM_171010) is another VGAM1126 host target gene. LOC257054 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257054 BINDING SITE, designated SEQ ID:45780, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40749] Another function of VGAM1126 is therefore inhibition of LOC257054 (Accession XM_171010). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257054. LOC51236 (Accession NM_016458) is another VGAM1126 host target gene. LOC51236 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51236 BINDING SITE, designated SEQ ID:18570, to the

nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40750] Another function of VGAM1126 is therefore inhibition of LOC51236 (Accession NM_016458). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51236. LOC51308 (Accession NM_016606) is another VGAM1126 host target gene. LOC51308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51308 BINDING SITE, designated SEQ ID:18707, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40751] Another function of VGAM1126 is therefore inhibition of LOC51308 (Accession NM_016606). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51308. LOC56961 (Accession XM_031857) is another VGAM1126 host target gene. LOC56961 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by LOC56961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56961 BINDING SITE, designated SEQ ID:31505, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40752] Another function of VGAM1126 is therefore inhibition of LOC56961 (Accession XM_031857). Accordingly, utilities of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56961. LOC91373 (Accession XM_038063) is another VGAM1126 host target gene. LOC91373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91373 BINDING SITE, designated SEQ ID:32751, to the nucleotide sequence of VGAM1126 RNA, herein designated VGAM RNA, also designated SEQ ID:3837.

[40753] Another function of VGAM1126 is therefore inhibition of LOC91373 (Accession XM_038063). Accordingly, utilities

of VGAM1126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91373. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1127 (VGAM1127) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40754] VGAM1127 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1127 was detected is described hereinabove with reference to Figs. 1-8.

[40755] VGAM1127 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40756] VGAM1127 gene encodes a VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1127 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1127 precursor RNA is designated SEQ ID:1113, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1113 is located at position 1512 relative to the genome of Barley Stripe Mosaic Virus.

[40757] VGAM1127 precursor RNA folds onto itself, forming VGAM1127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40758] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1127 folded precursor RNA into VGAM1127 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1127 RNA is designated SEQ ID:3838, and

is provided hereinbelow with reference to the sequence listing part.

[40759] VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1127 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40760] VGAM1127 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1127 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1127 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40761] The complementary binding of VGAM1127 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1127 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1127 host target RNA into VGAM1127 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40762] It is appreciated that VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1127 host target genes. The mRNA of each one of this plurality of VGAM1127 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1127 RNA, herein designated VGAM RNA, and which when bound by VGAM1127 RNA causes inhibition of translation of respective one or more VGAM1127 host target proteins.

[40763] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1127 gene, herein designated VGAM GENE, on one or more VGAM1127 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40764] It is yet further appreciated that a function of VGAM1127 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1127 correlate with, and may be deduced from, the identity of the host target genes which VGAM1127 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40765] Nucleotide sequences of the VGAM1127 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1127 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1127 are further described hereinbelow with reference to Table 1.

[40766] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1127 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1127 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40767] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1127 gene, herein designated VGAM is inhibition of expression of VGAM1127 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1127 correlate with, and may be deduced from, the identity of the target genes which VGAM1127 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40768] Coronin, Actin Binding Protein, 2A (CORO2A, Accession NM_052820) is a VGAM1127 host target gene. CORO2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORO2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO2A BINDING SITE, designated SEQ ID:27408, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40769] A function of VGAM1127 is therefore inhibition of Coronin, Actin Binding Protein, 2A (CORO2A, Accession NM_052820). Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CORO2A. Fibulin 5 (FBLN5,

Accession NM_006329) is another VGAM1127 host target gene. FBLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN5 BINDING SITE, designated SEQ ID:13021, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40770] Another function of VGAM1127 is therefore inhibition of Fibulin 5 (FBLN5, Accession NM_006329), a gene which promotes adhesion of endothelial cells through interaction of integrins and the rgd motif. Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN5. The function of FBLN5 has been established by previous studies. In sequence analysis of mouse fibulin-1 (FBLN1; 135820), Pan et al. (1993) obtained several similar cDNA clones that suggested the existence of a second isoform. Detailed study of the sequence predicted a novel and longer protein, fibulin-2. The protein predicted from the cDNA obtained from a mouse fibroblast library consisted

of a 1,195-residue polypeptide preceded by a 26-residue signal peptide. Except for 2 additional EGF-like repeats, the COOH-terminal region showed 43% sequence identity with fibulin-1. The NH₂-terminal 408 residues, unique to fibulin-2, showed no sequence homology to other known proteins and presumably formed 2 additional domains that differ in their cysteine content. Recombinant fibulin-2 was produced and secreted by human cell clones as a disulfide-bonded trimer. No significant immunologic cross-reactivity could be detected between fibulin-1 and fibulin-2. Production of fibulin-2 was demonstrated by Northern blots and radioimmunoassay in fibroblasts but not in several tumor cell lines. Together with the observation that the serum level of fibulin-2 is 1,000-fold lower than that of fibulin-1, the data indicated that the 2 isoforms are not always coordinately expressed. Zhang et al. (1994) isolated and sequenced a 4.1-kb human fibulin-2 cDNA, which encoded a mature protein of 1,157 amino acids preceded by a 27-residue signal sequence. The predicted polypeptide was found to contain 3 consecutive anaphylatoxin-related segments (domain I) in its central region followed by 10 EGF-like repeats (domain II), 9 of which had a consensus sequence for calcium binding. The

amino acid sequences of human and mouse fibulin-2 shared approximately 90% identity in 3 domains but only 62% in another. Northern blot analysis of mRNA from various human tissues revealed an abundant 4.5-kb transcript in heart, placenta, and ovary tissue. The expression pattern differed from that of fibulin-1. By isotopic in situ hybridization, Zhang et al. (1994) mapped the FBLN2 gene to 3p25-p24 in the human and to chromosome 6 in the D-E region in the mouse. Using 2 polymorphisms in the FBLN2 gene, Collod et al. (1996) excluded FBLN2 as the site of the mutation causing type II Marfan syndrome (OMIM Ref. No. 154705), which maps to the same region of 3p. Using conformation-sensitive gel electrophoresis and direct sequencing of PCR products to screen for mutations in the cDNA for FBLN2, Kuivaniemi et al. (1998) studied 11 patients with abdominal aortic aneurysms and 2 controls. They found a total of 14 single-base sequence variations but these did not segregate with abdominal aortic aneurysms in families.

[40771] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40772] Collod, G.; Chu, M.-L.; Sasaki, T.; Coulon, M.; Timpl, R.;

Renkart, L.; Weissenbach, J.; Jondeau, G.; Bourdarias, J. P.; Junien, C.; Boileau, C. : Fibulin-2: genetic mapping and exclusion as a candidate gene in Marfan syndrome type 2. *Europ. J. Hum. Genet.* 4: 292-295, 1996. ; and

[40773] Kuivaniemi, H.; Marshall, A.; Ganguly, A.; Chu, M.-L.; Abbott, W. M.; Tromp, G. : Fibulin-2 exhibits high degree of variability, but no structural changes concordant with abdominal aort.

[40774] Further studies establishing the function and utilities of FBLN5 are found in John Hopkins OMIM database record ID 604580, and in cited publications numbered 4937-4940 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM_020472) is another VGAM1127 host target gene. PIGA BINDING SITE1 through PIGA BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIGA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGA BINDING SITE1 through PIGA BINDING SITE3, designated SEQ ID:21708, SEQ ID:8497

and SEQ ID:21715 respectively, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40775] Another function of VGAM1127 is therefore inhibition of Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM_020472). Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGA. Apolipoprotein L, 2 (APOL2, Accession NM_030882) is another VGAM1127 host target gene. APOL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL2 BINDING SITE, designated SEQ ID:25159, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40776] Another function of VGAM1127 is therefore inhibition of Apolipoprotein L, 2 (APOL2, Accession NM_030882). Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL2. JDD1 (Accession XM_032515) is another VGAM1127 host target gene. JDD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JDD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JDD1 BINDING SITE, designated SEQ ID:31668, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40777] Another function of VGAM1127 is therefore inhibition of JDD1 (Accession XM_032515). Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JDD1. Mab-21-like 2 (C. elegans) (MAB21L2, Accession NM_006439) is another VGAM1127 host target gene. MAB21L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAB21L2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L2 BINDING SITE, designated SEQ ID:13152, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40778] Another function of VGAM1127 is therefore inhibition of Mab-21-like 2 (*C. elegans*) (MAB21L2, Accession NM_006439). Accordingly, utilities of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L2. LOC254413 (Accession XM_173141) is another VGAM1127 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46398, to the nucleotide sequence of VGAM1127 RNA, herein designated VGAM RNA, also designated SEQ ID:3838.

[40779] Another function of VGAM1127 is therefore inhibition of LOC254413 (Accession XM_173141). Accordingly, utilities

of VGAM1127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1128 (VGAM1128) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40780] VGAM1128 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1128 was detected is described hereinabove with reference to Figs. 1-8.

[40781] VGAM1128 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40782] VGAM1128 gene encodes a VGAM1128 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1128 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1128 precursor RNA is designated SEQ ID:1114, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1114 is located at position 2166 relative to the genome of Barley Stripe Mosaic Virus.

[40783] VGAM1128 precursor RNA folds onto itself, forming VGAM1128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40784] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1128 folded precursor RNA into VGAM1128 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1128 RNA is designated SEQ ID:3839, and

is provided hereinbelow with reference to the sequence listing part.

[40785] VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1128 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40786] VGAM1128 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1128 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1128 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40787] The complementary binding of VGAM1128 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1128 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1128 host target RNA into VGAM1128 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40788] It is appreciated that VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1128 host target genes. The mRNA of each one of this plurality of VGAM1128 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1128 RNA, herein designated VGAM RNA, and which when bound by VGAM1128 RNA causes inhibition of translation of respective one or more VGAM1128 host target proteins.

[40789] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1128 gene, herein designated VGAM GENE, on one or more VGAM1128 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40790] It is yet further appreciated that a function of VGAM1128 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1128 correlate with, and may be deduced from, the identity of the host target genes which VGAM1128 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40791] Nucleotide sequences of the VGAM1128 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1128 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1128 are further described hereinbelow with reference to Table 1.

[40792] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1128 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1128 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40793] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1128 gene, herein designated VGAM is inhibition of expression of VGAM1128 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1128 correlate with, and may be deduced from, the identity of the target genes which VGAM1128 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40794] Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM_001408) is a VGAM1128 host target gene. CELSR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CELSR2 BINDING SITE, designated SEQ ID:7105, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40795] A function of VGAM1128 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM_001408), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM1128 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with CELSR2. The function of CELSR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. Leptin (obesity homolog, mouse) (LEP, Accession NM_000230) is another VGAM1128 host target gene. LEP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEP BINDING SITE, designated SEQ ID:5736, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40796] Another function of VGAM1128 is therefore inhibition of Leptin (obesity homolog, mouse) (LEP, Accession NM_000230). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP. Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600) is another VGAM1128 host target gene. TCF3 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by TCF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF3 BINDING SITE, designated SEQ ID:35008, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40797] Another function of VGAM1128 is therefore inhibition of Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600), a gene which plays major roles in determining tissue-specific cell fate during embryogenesis. Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF3. The function of TCF3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM_080603) is another VGAM1128 host target gene. C20orf162 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C20orf162, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf162 BINDING SITE, designated SEQ ID:27921, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40798] Another function of VGAM1128 is therefore inhibition of Chromosome 20 Open Reading Frame 162 (C20orf162, Accession NM_080603). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf162. DKFZp434K1210 (Accession NM_017606) is another VGAM1128 host target gene. DKFZp434K1210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434K1210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434K1210 BINDING SITE, designated SEQ ID:19100, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40799] Another function of VGAM1128 is therefore inhibition of

DKFZp434K1210 (Accession NM_017606). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434K1210. FLJ10737 (Accession NM_018198) is another VGAM1128 host target gene. FLJ10737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10737 BINDING SITE, designated SEQ ID:20063, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40800] Another function of VGAM1128 is therefore inhibition of FLJ10737 (Accession NM_018198). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10737. FLJ10956 (Accession NM_018283) is another VGAM1128 host target gene. FLJ10956 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10956, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10956 BINDING SITE, designated SEQ ID:20277, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40801] Another function of VGAM1128 is therefore inhibition of FLJ10956 (Accession NM_018283). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10956. Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1, Accession NM_002056) is another VGAM1128 host target gene. GFPT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFPT1 BINDING SITE, designated SEQ ID:7819, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40802] Another function of VGAM1128 is therefore inhibition of Glutamine-fructose-6-phosphate Transaminase 1 (GFPT1, Accession NM_002056). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GFPT1. G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776) is another VGAM1128 host target gene. GIT2 BINDING SITE1 through GIT2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GIT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE1 through GIT2 BINDING SITE3, designated SEQ ID:16597, SEQ ID:27692 and SEQ ID:27679 respectively, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40803] Another function of VGAM1128 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. MGC13198 (Accession NM_032690) is another VGAM1128 host target gene. MGC13198 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC13198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13198 BINDING SITE, designated SEQ ID:26410, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40804] Another function of VGAM1128 is therefore inhibition of MGC13198 (Accession NM_032690). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13198. SPEC1 (Accession NM_020239) is another VGAM1128 host target gene. SPEC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPEC1 BINDING SITE, designated SEQ ID:21507, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40805] Another function of VGAM1128 is therefore inhibition of SPEC1 (Accession NM_020239). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPEC1.

LOC146819 (Accession XM_085605) is another VGAM1128 host target gene. LOC146819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146819 BINDING SITE, designated SEQ ID:38253, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40806] Another function of VGAM1128 is therefore inhibition of LOC146819 (Accession XM_085605). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146819. LOC146821 (Accession XM_085597) is another VGAM1128 host target gene. LOC146821 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146821 BINDING SITE, designated SEQ ID:38251, to the nucleotide sequence of VGAM1128 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3839.

[40807] Another function of VGAM1128 is therefore inhibition of LOC146821 (Accession XM_085597). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146821. LOC153218 (Accession XM_087628) is another VGAM1128 host target gene. LOC153218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153218 BINDING SITE, designated SEQ ID:39364, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40808] Another function of VGAM1128 is therefore inhibition of LOC153218 (Accession XM_087628). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153218. LOC253187 (Accession XM_173139) is another VGAM1128 host target gene. LOC253187 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253187, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253187 BINDING SITE, designated SEQ ID:46393, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40809] Another function of VGAM1128 is therefore inhibition of LOC253187 (Accession XM_173139). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253187. LOC253613 (Accession XM_171225) is another VGAM1128 host target gene. LOC253613 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253613 BINDING SITE, designated SEQ ID:46006, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40810] Another function of VGAM1128 is therefore inhibition of LOC253613 (Accession XM_171225). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253613. LOC54466 (Accession NM_019003) is another VGAM1128 host target gene. LOC54466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54466 BINDING SITE, designated SEQ ID:21075, to the nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40811] Another function of VGAM1128 is therefore inhibition of LOC54466 (Accession NM_019003). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54466. LOC91963 (Accession XM_041902) is another VGAM1128 host target gene. LOC91963 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91963 BINDING SITE, designated SEQ ID:33628, to the

nucleotide sequence of VGAM1128 RNA, herein designated VGAM RNA, also designated SEQ ID:3839.

[40812] Another function of VGAM1128 is therefore inhibition of LOC91963 (Accession XM_041902). Accordingly, utilities of VGAM1128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91963. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1129 (VGAM1129) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40813] VGAM1129 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1129 was detected is described hereinabove with reference to Figs. 1–8.

[40814] VGAM1129 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40815] VGAM1129 gene encodes a VGAM1129 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1129 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1129 precursor RNA is designated SEQ ID:1115, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1115 is located at position 2771 relative to the genome of Barley Stripe Mosaic Virus.

[40816] VGAM1129 precursor RNA folds onto itself, forming VGAM1129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40817] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1129 folded precursor RNA into VGAM1129 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1129 RNA is designated SEQ ID:3840, and is provided hereinbelow with reference to the sequence listing part.

[40818] VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1129 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40819] VGAM1129 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1129 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1129 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40820] The complementary binding of VGAM1129 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1129 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1129 host target RNA into VGAM1129 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40821] It is appreciated that VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1129 host target genes. The mRNA of each one of this plurality of VGAM1129 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1129 RNA, herein designated VGAM RNA, and which when bound by VGAM1129 RNA causes inhibition of translation of respective one or more VGAM1129 host target proteins.

[40822] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1129 gene, herein designated VGAM GENE, on one or more VGAM1129 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[40823] It is yet further appreciated that a function of VGAM1129 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1129 correlate with, and may be deduced from, the identity of the host target genes which VGAM1129 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40824] Nucleotide sequences of the VGAM1129 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1129 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1129 are further described hereinbelow with reference to Table 1.

[40825] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1129 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1129 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40826] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1129 gene, herein designated VGAM is inhibition of expression of VGAM1129 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1129 correlate with, and may be deduced from, the identity of the target genes which VGAM1129 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40827] Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM_004393) is a VGAM1129 host target gene. DAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE, designated SEQ ID:10633, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40828] A function of VGAM1129 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1,

Accession NM_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAG1. The function of DAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1095.ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069) is another VGAM1129 host target gene. ATP1B4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B4 BINDING SITE, designated SEQ ID:14327, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40829] Another function of VGAM1129 is therefore inhibition of ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ATP1B4. DKFZP564C196 (Accession XM_046405) is another VGAM1129 host target gene. DKFZP564C196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564C196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C196 BINDING SITE, designated SEQ ID:34712, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40830] Another function of VGAM1129 is therefore inhibition of DKFZP564C196 (Accession XM_046405). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C196. PP1057 (Accession NM_031285) is another VGAM1129 host target gene. PP1057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

PP1057 BINDING SITE, designated SEQ ID:25311, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40831] Another function of VGAM1129 is therefore inhibition of PP1057 (Accession NM_031285). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1057. LOC143920 (Accession XM_084658) is another VGAM1129 host target gene. LOC143920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143920 BINDING SITE, designated SEQ ID:37642, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40832] Another function of VGAM1129 is therefore inhibition of LOC143920 (Accession XM_084658). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143920. LOC154881 (Accession XM_088063) is another VGAM1129 host target gene. LOC154881 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39499, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40833] Another function of VGAM1129 is therefore inhibition of LOC154881 (Accession XM_088063). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154881. LOC255152 (Accession XM_173310) is another VGAM1129 host target gene. LOC255152 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255152 BINDING SITE, designated SEQ ID:46534, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40834] Another function of VGAM1129 is therefore inhibition of

LOC255152 (Accession XM_173310). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255152. LOC255481 (Accession XM_170489) is another VGAM1129 host target gene. LOC255481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255481 BINDING SITE, designated SEQ ID:45330, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40835] Another function of VGAM1129 is therefore inhibition of LOC255481 (Accession XM_170489). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255481. LOC91301 (Accession XM_037564) is another VGAM1129 host target gene. LOC91301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC91301 BINDING SITE, designated SEQ ID:32648, to the nucleotide sequence of VGAM1129 RNA, herein designated VGAM RNA, also designated SEQ ID:3840.

[40836] Another function of VGAM1129 is therefore inhibition of LOC91301 (Accession XM_037564). Accordingly, utilities of VGAM1129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1130 (VGAM1130) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40837] VGAM1130 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1130 was detected is described hereinabove with reference to Figs. 1–8.

[40838] VGAM1130 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[40839] VGAM1130 gene encodes a VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1130 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1130 precursor RNA is designated SEQ ID:1116, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1116 is located at position 3018 relative to the genome of Barley Stripe Mosaic Virus.

[40840] VGAM1130 precursor RNA folds onto itself, forming VGAM1130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40841] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1130 folded precursor RNA into VGAM1130 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1130 RNA is designated SEQ ID:3841, and is provided hereinbelow with reference to the sequence listing part.

[40842] VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1130 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40843] VGAM1130 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1130 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1130 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40844] The complementary binding of VGAM1130 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1130 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1130 host target RNA into VGAM1130 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40845] It is appreciated that VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1130 host target genes. The mRNA of each one of this plurality of VGAM1130 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1130 RNA, herein designated VGAM RNA, and which when bound by VGAM1130 RNA causes inhibition of translation of respective one or more VGAM1130 host target proteins.

[40846] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1130 gene, herein designated VGAM GENE, on one or more VGAM1130 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40847] It is yet further appreciated that a function of VGAM1130 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1130 correlate with, and may be deduced from, the identity of the host target genes which VGAM1130 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40848] Nucleotide sequences of the VGAM1130 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1130 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1130 are further described hereinbelow with reference to Table 1.

[40849] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1130 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1130 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40850] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1130 gene, herein designated VGAM is inhibition of expression of VGAM1130 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1130 correlate with, and may be deduced from, the identity of the target genes which VGAM1130 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40851] NDRG Family Member 2 (NDRG2, Accession NM_016250) is a VGAM1130 host target gene. NDRG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDRG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG2 BINDING SITE, designated SEQ ID:18378, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ ID:3841.

[40852] A function of VGAM1130 is therefore inhibition of NDRG Family Member 2 (NDRG2, Accession NM_016250), a gene which belongs to the ndrg family. Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG2. The function of NDRG2 has been established by previous studies. Van Belzen et al. (1997) and Piquemal et al. (1999) demonstrated the existence of an Ndr gene family in mouse and human. Using the novel mouse sequences of Ndr2 and Ndr3 to search the human genome databases, Kalaydjieva et al. (2000) identified the homologous human genes, which they referred as NDRG2 and NDRG3 (OMIM Ref. No. 605273). Kalaydjieva et al. (2000) stated that the 3 known human NDRG proteins show considerable homology: 54% amino acid sequence identity between NDRG1 (OMIM Ref. No. 605262) and NDRG2, 67% between NDRG1 and NDRG3, and 58% between NDRG2 and NDRG3. By radiation hybrid analysis, Kalaydjieva et al. (2000) mapped the NDRG2 gene to chromosome 14q11.2.

[40853] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40854] Kalaydjieva, L.; Gresham, D.; Gooding, R.; Heather, L.;

Baas, F.; de Jonge, R.; Blechschmidt, K.; Angelicheva, D.; Chandler, D.; Worsley, P.; Rosenthal, A.; King, R. H. M.; Thomas, P. K. : N-myc downstream-regulated gene 1 is mutated in hereditary motor and sensory neuropathy-Lom. Am. J. Hum. Genet. 67: 47-58, 2000. ; and

[40855] Piquemal, D.; Joulia, D.; Balaguer, P.; Basset, A.; Marti, J.; Commes, T. : Differential expression of the RTP/Drg1/Ndr1 gene product in proliferating and growth arrested cells. Biochi.

[40856] Further studies establishing the function and utilities of NDRG2 are found in John Hopkins OMIM database record ID 605272, and in cited publications numbered 135 and 6612 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. AD022 (Accession XM_165725) is another VGAM1130 host target gene. AD022 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AD022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AD022 BINDING SITE, designated SEQ ID:43737, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ

ID:3841.

[40857] Another function of VGAM1130 is therefore inhibition of AD022 (Accession XM_165725). Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AD022. KIAA0534 (Accession XM_049349) is another VGAM1130 host target gene. KIAA0534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0534 BINDING SITE, designated SEQ ID:35384, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ ID:3841.

[40858] Another function of VGAM1130 is therefore inhibition of KIAA0534 (Accession XM_049349). Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0534. Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_014835) is another VGAM1130 host target gene. OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated re-

gions of mRNA encoded by OSBPL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2, designated SEQ ID:16848 and SEQ ID:29316 respectively, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ ID:3841.

[40859] Another function of VGAM1130 is therefore inhibition of Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_014835). Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL2. TUBB5 (Accession NM_006087) is another VGAM1130 host target gene. TUBB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUBB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUBB5 BINDING SITE, designated SEQ ID:12729, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ ID:3841.

[40860] Another function of VGAM1130 is therefore inhibition of TUBB5 (Accession NM_006087). Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUBB5. LOC157657 (Accession XM_088352) is another VGAM1130 host target gene. LOC157657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157657 BINDING SITE, designated SEQ ID:39625, to the nucleotide sequence of VGAM1130 RNA, herein designated VGAM RNA, also designated SEQ ID:3841.

[40861] Another function of VGAM1130 is therefore inhibition of LOC157657 (Accession XM_088352). Accordingly, utilities of VGAM1130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157657. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1131 (VGAM1131) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[40862] VGAM1131 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1131 was detected is described hereinabove with reference to Figs. 1-8.

[40863] VGAM1131 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40864] VGAM1131 gene encodes a VGAM1131 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1131 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1131 precursor RNA is designated SEQ ID:1117, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1117 is located at position 1786 relative to the genome of Barley Stripe Mosaic Virus.

[40865] VGAM1131 precursor RNA folds onto itself, forming VGAM1131 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40866] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1131 folded precursor RNA into VGAM1131 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1131 RNA is designated SEQ ID:3842, and is provided hereinbelow with reference to the sequence listing part.

[40867] VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1131 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40868] VGAM1131 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1131 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1131 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[40869] The complementary binding of VGAM1131 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1131 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1131 host target RNA into VGAM1131 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40870] It is appreciated that VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1131 host target genes. The mRNA of each one of this plurality of VGAM1131 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1131 RNA, herein designated VGAM RNA, and which when bound by VGAM1131 RNA causes inhibition of translation of respective one or more VGAM1131 host target proteins.

[40871] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1131 gene, herein designated VGAM GENE, on one or more VGAM1131 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40872] It is yet further appreciated that a function of VGAM1131 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1131 correlate with, and may be deduced from, the identity of the host target genes which VGAM1131 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[40873] Nucleotide sequences of the VGAM1131 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1131 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1131 are further described hereinbelow with reference to Table 1.

[40874] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1131 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1131 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40875] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1131 gene, herein designated VGAM is inhibition of expression of VGAM1131 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1131 correlate with, and may be deduced from, the identity of the target genes which VGAM1131 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40876] Myotubularin Related Protein 8 (MTMR8, Accession NM_015458) is a VGAM1131 host target gene. MTMR8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTMR8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR8 BINDING SITE, designated SEQ ID:17751, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40877] A function of VGAM1131 is therefore inhibition of Myotubularin Related Protein 8 (MTMR8, Accession NM_015458), a gene which could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR8. The function of MTMR8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM379.FLJ10520 (Accession NM_018124) is another VGAM1131 host target gene. FLJ10520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10520, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10520 BINDING SITE, designated SEQ ID:19909, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40878] Another function of VGAM1131 is therefore inhibition of FLJ10520 (Accession NM_018124). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10520. FLJ31564 (Accession NM_144720) is another VGAM1131 host target gene. FLJ31564 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ31564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31564 BINDING SITE, designated SEQ ID:29541, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40879] Another function of VGAM1131 is therefore inhibition of FLJ31564 (Accession NM_144720). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ31564. MGC13114 (Accession NM_032366) is another VGAM1131 host target gene. MGC13114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13114 BINDING SITE, designated SEQ ID:26153, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40880] Another function of VGAM1131 is therefore inhibition of MGC13114 (Accession NM_032366). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13114. LOC145836 (Accession XM_096881) is another VGAM1131 host target gene. LOC145836 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145836 BINDING SITE, designated SEQ ID:40614, to

the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40881] Another function of VGAM1131 is therefore inhibition of LOC145836 (Accession XM_096881). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145836. LOC221466 (Accession XM_168087) is another VGAM1131 host target gene. LOC221466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221466 BINDING SITE, designated SEQ ID:44996, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40882] Another function of VGAM1131 is therefore inhibition of LOC221466 (Accession XM_168087). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221466. LOC57086 (Accession NM_020351) is another VGAM1131 host target gene. LOC57086 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC57086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57086 BINDING SITE, designated SEQ ID:21617, to the nucleotide sequence of VGAM1131 RNA, herein designated VGAM RNA, also designated SEQ ID:3842.

[40883] Another function of VGAM1131 is therefore inhibition of LOC57086 (Accession NM_020351). Accordingly, utilities of VGAM1131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57086. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1132 (VGAM1132) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40884] VGAM1132 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1132 was detected is described hereinabove with reference to Figs. 1-8.

[40885] VGAM1132 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Barley Stripe Mosaic Virus. VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40886] VGAM1132 gene encodes a VGAM1132 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1132 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1132 precursor RNA is designated SEQ ID:1118, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1118 is located at position 849 relative to the genome of Barley Stripe Mosaic Virus.

[40887] VGAM1132 precursor RNA folds onto itself, forming VGAM1132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40888] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1132 folded precursor RNA into VGAM1132 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1132 RNA is designated SEQ ID:3843, and is provided hereinbelow with reference to the sequence listing part.

[40889] VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1132 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40890] VGAM1132 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1132 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1132 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40891] The complementary binding of VGAM1132 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1132 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1132

host target RNA into VGAM1132 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40892] It is appreciated that VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1132 host target genes. The mRNA of each one of this plurality of VGAM1132 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1132 RNA, herein designated VGAM RNA, and which when bound by VGAM1132 RNA causes inhibition of translation of respective one or more VGAM1132 host target proteins.

[40893] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1132 gene, herein designated VGAM GENE, on one or more VGAM1132 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40894] It is yet further appreciated that a function of VGAM1132 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1132 correlate with, and may be deduced from, the identity of the host target genes which VGAM1132 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40895] Nucleotide sequences of the VGAM1132 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1132 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1132 are further

described hereinbelow with reference to Table 1.

[40896] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1132 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1132 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40897] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1132 gene, herein designated VGAM is inhibition of expression of VGAM1132 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1132 correlate with, and may be deduced from, the identity of the target genes which VGAM1132 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40898] Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is a VGAM1132 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FGF2 BINDING SITE, designated SEQ ID:7736, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40899] A function of VGAM1132 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Lactate Dehydrogenase B (LDHB, Accession NM_002300) is another VGAM1132 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8089, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40900] Another function of VGAM1132 is therefore inhibition of

Lactate Dehydrogenase B (LDHB, Accession NM_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM273. Protocadherin 11 X-linked (PCDH11X, Accession NM_032968) is another VGAM1132 host target gene. PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11X, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2, designated SEQ ID:26794 and SEQ ID:26809 respectively, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40901] Another function of VGAM1132 is therefore inhibition of Protocadherin 11 X-linked (PCDH11X, Accession NM_032968), a gene which is thought to play a fundamental role in cell-cell recognition essential for the seg-

mental development and function of the central nervous system. Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11X. The function of PCDH11X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.AFAP (Accession NM_021638) is another VGAM1132 host target gene. AFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AFAP BINDING SITE, designated SEQ ID:22294, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40902] Another function of VGAM1132 is therefore inhibition of AFAP (Accession NM_021638). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AFAP. FLJ12484 (Accession NM_022767) is another VGAM1132 host target gene. FLJ12484 BINDING SITE1 and FLJ12484

BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 and FLJ12484 BINDING SITE2, designated SEQ ID:23017 and SEQ ID:34515 respectively, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40903] Another function of VGAM1132 is therefore inhibition of FLJ12484 (Accession NM_022767). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. KIAA0040 (Accession NM_014656) is another VGAM1132 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16098, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40904] Another function of VGAM1132 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. PRO1048 (Accession NM_018497) is another VGAM1132 host target gene. PRO1048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1048 BINDING SITE, designated SEQ ID:20562, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40905] Another function of VGAM1132 is therefore inhibition of PRO1048 (Accession NM_018497). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1048. LOC149117 (Accession XM_097587) is another VGAM1132 host target gene. LOC149117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149117, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149117 BINDING SITE, designated SEQ ID:40955, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40906] Another function of VGAM1132 is therefore inhibition of LOC149117 (Accession XM_097587). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149117. LOC220929 (Accession XM_166134) is another VGAM1132 host target gene. LOC220929 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220929 BINDING SITE, designated SEQ ID:43929, to the nucleotide sequence of VGAM1132 RNA, herein designated VGAM RNA, also designated SEQ ID:3843.

[40907] Another function of VGAM1132 is therefore inhibition of LOC220929 (Accession XM_166134). Accordingly, utilities of VGAM1132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220929. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1133 (VGAM1133) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40908] VGAM1133 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1133 was detected is described hereinabove with reference to Figs. 1–8.

[40909] VGAM1133 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Maize Rayado Fino Virus. VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40910] VGAM1133 gene encodes a VGAM1133 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1133 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1133 precursor RNA is designated SEQ ID:1119, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1119 is located at position 5936 relative to the genome of Maize Rayado Fino Virus.

- [40911] VGAM1133 precursor RNA folds onto itself, forming VGAM1133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [40912] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1133 folded precursor RNA into VGAM1133 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1133 RNA is designated SEQ ID:3844, and is provided hereinbelow with reference to the sequence listing part.

[40913] VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1133 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[40914] VGAM1133 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1133 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1133 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40915] The complementary binding of VGAM1133 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1133 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1133 host target RNA into VGAM1133 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40916] It is appreciated that VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1133 host target genes. The mRNA of each one of this plurality of VGAM1133 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1133 RNA, herein designated VGAM RNA, and which when bound by VGAM1133 RNA causes

inhibition of translation of respective one or more VGAM1133 host target proteins.

[40917] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1133 gene, herein designated VGAM GENE, on one or more VGAM1133 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40918] It is yet further appreciated that a function of VGAM1133 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1133 include diagnosis, prevention and

treatment of viral infection by Maize Rayado Fino Virus. Specific functions, and accordingly utilities, of VGAM1133 correlate with, and may be deduced from, the identity of the host target genes which VGAM1133 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40919] Nucleotide sequences of the VGAM1133 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1133 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1133 are further described hereinbelow with reference to Table 1.

[40920] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1133 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1133 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40921] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1133 gene, herein designated VGAM is inhibition of expression of VGAM1133 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1133 correlate with, and may be deduced from, the identity of the target genes which VGAM1133 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40922] Solute Carrier Family 2 (facilitated glucose transporter), Member 1 (SLC2A1, Accession NM_006516) is a VGAM1133 host target gene. SLC2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A1 BINDING SITE, designated SEQ ID:13264, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40923] A function of VGAM1133 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 1 (SLC2A1, Accession NM_006516). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A1. Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945) is another VGAM1133

host target gene. C21orf25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf25 BINDING SITE, designated SEQ ID:31800, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40924] Another function of VGAM1133 is therefore inhibition of Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf25.

FLJ10849 (Accession NM_018243) is another VGAM1133 host target gene. FLJ10849 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10849, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10849 BINDING SITE, designated SEQ ID:20204, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3844.

[40925] Another function of VGAM1133 is therefore inhibition of FLJ10849 (Accession NM_018243). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10849. Musculin (activated B-cell factor-1) (MSC, Accession XM_084266) is another VGAM1133 host target gene. MSC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSC BINDING SITE, designated SEQ ID:37533, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40926] Another function of VGAM1133 is therefore inhibition of Musculin (activated B-cell factor-1) (MSC, Accession XM_084266). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSC. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737) is another VGAM1133 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16389, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40927] Another function of VGAM1133 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. Zinc Finger Protein 337 (ZNF337, Accession XM_042807) is another VGAM1133 host target gene. ZNF337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF337 BINDING SITE, designated SEQ ID:33770, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ

ID:3844.

[40928] Another function of VGAM1133 is therefore inhibition of Zinc Finger Protein 337 (ZNF337, Accession XM_042807). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF337. LOC154834 (Accession XM_098621) is another VGAM1133 host target gene. LOC154834 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154834, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154834 BINDING SITE, designated SEQ ID:41730, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40929] Another function of VGAM1133 is therefore inhibition of LOC154834 (Accession XM_098621). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154834. LOC200720 (Accession XM_117264) is another VGAM1133 host target gene. LOC200720 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC200720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200720 BINDING SITE, designated SEQ ID:43342, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40930] Another function of VGAM1133 is therefore inhibition of LOC200720 (Accession XM_117264). Accordingly, utilities of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200720. LOC91461 (Accession XM_038576) is another VGAM1133 host target gene. LOC91461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91461 BINDING SITE, designated SEQ ID:32869, to the nucleotide sequence of VGAM1133 RNA, herein designated VGAM RNA, also designated SEQ ID:3844.

[40931] Another function of VGAM1133 is therefore inhibition of LOC91461 (Accession XM_038576). Accordingly, utilities

of VGAM1133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91461. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1134 (VGAM1134) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40932] VGAM1134 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1134 was detected is described hereinabove with reference to Figs. 1-8.

[40933] VGAM1134 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Maize Rayado Fino Virus. VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40934] VGAM1134 gene encodes a VGAM1134 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1134 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1134 precursor RNA is designated SEQ ID:1120, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1120 is located at position 4286 relative to the genome of Maize Rayado Fino Virus.

- [40935] VGAM1134 precursor RNA folds onto itself, forming VGAM1134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [40936] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1134 folded precursor RNA into VGAM1134 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1134 RNA is designated SEQ ID:3845, and

is provided hereinbelow with reference to the sequence listing part.

[40937] VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1134 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[40938] VGAM1134 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1134 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1134 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40939] The complementary binding of VGAM1134 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1134 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1134 host target RNA into VGAM1134 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40940] It is appreciated that VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1134 host target genes. The mRNA of each one of this plurality of VGAM1134 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1134 RNA, herein designated VGAM RNA, and which when bound by VGAM1134 RNA causes inhibition of translation of respective one or more VGAM1134 host target proteins.

[40941] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1134 gene, herein designated VGAM GENE, on one or more VGAM1134 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40942] It is yet further appreciated that a function of VGAM1134 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1134 include diagnosis, prevention and treatment of viral infection by Maize Rayado Fino Virus. Specific functions, and accordingly utilities, of VGAM1134 correlate with, and may be deduced from, the identity of the host target genes which VGAM1134 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40943] Nucleotide sequences of the VGAM1134 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1134 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1134 are further described hereinbelow with reference to Table 1.

[40944] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1134 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1134 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[40945] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1134 gene, herein designated VGAM is inhibition of expression of VGAM1134 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1134 correlate with, and may be deduced from, the identity of the target genes which VGAM1134 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[40946] AWP1 (Accession NM_019006) is a VGAM1134 host target gene. AWP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AWP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AWP1 BINDING SITE, designated SEQ ID:21077, to the nucleotide sequence of VGAM1134 RNA, herein designated VGAM RNA, also designated SEQ ID:3845.

[40947] A function of VGAM1134 is therefore inhibition of AWP1 (Accession NM_019006). Accordingly, utilities of VGAM1134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AWP1. LOC199796 (Accession XM_058994) is another VGAM1134 host target gene. LOC199796 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by LOC199796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199796 BINDING SITE, designated SEQ ID:36806, to the nucleotide sequence of VGAM1134 RNA, herein designated VGAM RNA, also designated SEQ ID:3845.

[40948] Another function of VGAM1134 is therefore inhibition of LOC199796 (Accession XM_058994). Accordingly, utilities of VGAM1134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199796. LOC257464 (Accession XM_116972) is another VGAM1134 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43163, to the nucleotide sequence of VGAM1134 RNA, herein designated VGAM RNA, also designated SEQ ID:3845.

[40949] Another function of VGAM1134 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities

of VGAM1134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC51313 (Accession NM_016613) is another VGAM1134 host target gene. LOC51313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51313 BINDING SITE, designated SEQ ID:18718, to the nucleotide sequence of VGAM1134 RNA, herein designated VGAM RNA, also designated SEQ ID:3845.

[40950] Another function of VGAM1134 is therefore inhibition of LOC51313 (Accession NM_016613). Accordingly, utilities of VGAM1134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51313. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1135 (VGAM1135) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[40951] VGAM1135 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1135 was detected is described hereinabove with reference to Figs. 1-8.

[40952] VGAM1135 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Maize Rayado Fino Virus. VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[40953] VGAM1135 gene encodes a VGAM1135 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1135 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1135 precursor RNA is designated SEQ ID:1121, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1121 is located at position 1316 relative to the genome of Maize Rayado Fino Virus.

[40954] VGAM1135 precursor RNA folds onto itself, forming VGAM1135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[40955] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1135 folded precursor RNA into VGAM1135 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1135 RNA is designated SEQ ID:3846, and is provided hereinbelow with reference to the sequence listing part.

[40956] VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1135 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[40957] VGAM1135 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1135 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1135 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[40958] The complementary binding of VGAM1135 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1135 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1135 host target RNA into VGAM1135 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[40959] It is appreciated that VGAM1135 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1135 host target genes. The mRNA of each one of this plurality of VGAM1135 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1135 RNA, herein designated VGAM RNA, and which when bound by VGAM1135 RNA causes inhibition of translation of respective one or more VGAM1135 host target proteins.

[40960] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1135 gene, herein designated VGAM GENE, on one or more VGAM1135 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[40961] It is yet further appreciated that a function of VGAM1135 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of viral infection by Maize Rayado Fino Virus. Specific functions, and accordingly utilities, of VGAM1135 correlate with, and may be deduced from, the identity of the host target genes which VGAM1135 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[40962] Nucleotide sequences of the VGAM1135 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1135 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1135 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1135 are further
described hereinbelow with reference to Table 1.

[40963] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1135 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1135 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[40964] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1135 gene, herein designated VGAM is
inhibition of expression of VGAM1135 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1135 correlate with, and may be deduced
from, the identity of the target genes which VGAM1135
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[40965] ATP-binding Cassette, Sub-family C (CFTR/MRP), Member
3 (ABCC3, Accession NM_020038) is a VGAM1135 host

target gene. ABCC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ABCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC3 BINDING SITE, designated SEQ ID:21294, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40966] A function of VGAM1135 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 3 (ABCC3, Accession NM_020038), a gene which may act as an inducible transporter in the biliary and intestinal excretion of organic anions. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC3. The function of ABCC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM505. ATP-binding Cassette, Sub-family D (ALD), Member 1 (ABCD1, Accession NM_000033) is another VGAM1135 host target gene. ABCD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by ABCD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD1 BINDING SITE, designated SEQ ID:5472, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40967] Another function of VGAM1135 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 1 (ABCD1, Accession NM_000033). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD1. Adrenergic, Alpha-2A-, Receptor (ADRA2A, Accession NM_000681) is another VGAM1135 host target gene. ADRA2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADRA2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADRA2A BINDING SITE, designated SEQ ID:6337, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40968] Another function of VGAM1135 is therefore inhibition of Adrenergic, Alpha-2A-, Receptor (ADRA2A, Accession NM_000681), a gene which mediates the effects of epinephrine and norepinephrine. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADRA2A. The function of ADRA2A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM602.UDP-Gal:betaGlcNAc Beta 1,4-Galactosyltransferase, Polypeptide 6 (B4GALT6, Accession XM_008799) is another VGAM1135 host target gene. B4GALT6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by B4GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT6 BINDING SITE, designated SEQ ID:30096, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40969] Another function of VGAM1135 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase,

Polypeptide 6 (B4GALT6, Accession XM_008799). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT6. Caspase Recruitment Domain Family, Member 10 (CARD10, Accession NM_014550) is another VGAM1135 host target gene. CARD10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD10 BINDING SITE, designated SEQ ID:15872, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40970] Another function of VGAM1135 is therefore inhibition of Caspase Recruitment Domain Family, Member 10 (CARD10, Accession NM_014550), a gene which functions to couple cell surface receptor stimulation and protein kinase C (see 176982) activation to the induction of NFkB through its interaction with BCL10. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD10. The function of CARD10 has been established by

previous studies. The caspase recruitment domain (CARD) is a protein module that consists of 6 or 7 antiparallel alpha helices. It participates in apoptosis signaling through highly specific protein-protein homophilic interactions. CARDS induce nuclear factor kappa-B (NFKB; 164011) activity through the IKK (e.g., IKBKB; 603258) complex. CARD9 (OMIM Ref. No. 607212), CARD10, CARD11 (OMIM Ref. No. 607210), and CARD14 (OMIM Ref. No. 607211) interact with BCL10 (OMIM Ref. No. 603517) and are involved in NFKB signaling complexes. Except for CARD9, these CARD proteins are members of the membrane-associated guanylate kinase (MAGUK) family. By coprecipitation analysis, McAllister-Lucas et al. (2001) showed that BIMP1, in the presence of BCL10, interacts with MALT1 (OMIM Ref. No. 604860) and cooperates in a signaling pathway through a CARD-mediated mechanism. Analysis of stimulated T cells suggested that BIMP1, through its interaction with BCL10, functions to couple cell surface receptor stimulation and protein kinase C (see OMIM Ref. No. 176982) activation to the induction of NFKB.

[40971] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [40972] Gaide, O.; Martinon, F.; Micheau, O.; Bonnet, D.; Thome, M.; Tschopp, J. : Carma1, a CARD-containing binding partner of Bcl10, induces Bcl10 phosphorylation and NF-kappa-B activation. FEBS Lett. 496: 121-127, 2001. ; and
- [40973] McAllister-Lucas, L. M.; Inohara, N.; Lucas, P. C.; Ruland, J.; Benito, A.; Li, Q.; Chen, S.; Chen, F. F.; Yamaoka, S.; Verma, I. M.; Mak, T. W.; Nunez, G. : Bimp1, a MAGUK family membe.
- [40974] Further studies establishing the function and utilities of CARD10 are found in John Hopkins OMIM database record ID 607209, and in cited publications numbered 5565-5567 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434) is another VGAM1135 host target gene. DAAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44329, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3846.

[40975] Another function of VGAM1135 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAAM2. The function of DAAM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Engrailed Homolog 2 (EN2, Accession NM_001427) is another VGAM1135 host target gene. EN2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN2 BINDING SITE, designated SEQ ID:7144, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40976] Another function of VGAM1135 is therefore inhibition of Engrailed Homolog 2 (EN2, Accession NM_001427), a gene which may be required for normal cerebellar devel-

opment; a homeobox protein, very strongly similar to murine En2. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN2. The function of EN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232.Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455) is another VGAM1135 host target gene. EXTL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10757, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40977] Another function of VGAM1135 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1135 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM806. Histone Deacetylase 7A (HDAC7A, Accession NM_015401) is another VGAM1135 host target gene. HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HDAC7A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC7A BINDING SITE1 and HDAC7A BINDING SITE2, designated SEQ ID:17712 and SEQ ID:18682 respectively, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40978] Another function of VGAM1135 is therefore inhibition of Histone Deacetylase 7A (HDAC7A, Accession NM_015401). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC7A. Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM_016059) is another VGAM1135 host target gene. PPIL1 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPIL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIL1 BINDING SITE, designated SEQ ID:18135, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40979] Another function of VGAM1135 is therefore inhibition of Peptidylprolyl Isomerase (cyclophilin)-like 1 (PPIL1, Accession NM_016059), a gene which catalyzes the cis-trans isomerization of proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIL1. The function of PPIL1 has been established by previous studies. Cyclophilin (see OMIM Ref. No. 123840), first identified as a protein with high binding affinity for the immunosuppressive agent cyclosporin A, is one of the most effective therapeutic agents for prevention of graft rejection after organ transplantation. Ozaki et al. (1996) isolated a human cDNA clone encoding a protein homologous to cyclophilins and showed that it is conserved in species ranging from hu-

man to prokaryotes. This cDNA contained an open reading frame of 498 nucleotides encoding a polypeptide of 166 amino acids. The predicted amino acid sequence had 41.6% homology to the human cyclophilins. Northern blot analysis indicated ubiquitous expression in adult human tissues, with the most abundant expression in heart and skeletal muscle. Ozaki et al. (1996) localized the PPIL1 gene to 2p23.3–p23.1 by FISH. However, Mann et al. (1998) assigned the PPIL1 gene to 6p21.1 by FISH and radiation hybrid mapping.

[40980] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40981] Mann, S. S.; Pettenati, M. J.; von Kap-herr, C.; Hart, T. C. : Reassignment of peptidyl prolyl isomerase-like 1 gene (PPIL1) to human chromosome region 6p21.1 by radiation hybrid mapping and fluorescence in situ hybridization. Cytogenet. Cell Genet. 83: 228–229, 1998. ; and

[40982] Ozaki, K.; Fujiwara, T.; Kawai, A.; Shimizu, F.; Takami, S.; Okuno, S.; Takeda, S.; Shimada, Y.; Nagata, M.; Watanabe, T.; Takaichi, A.; Takahashi, E.; Nakamura, Y.; Shin, S. : Cloning.

[40983] Further studies establishing the function and utilities of

PPIL1 are found in John Hopkins OMIM database record ID 601301, and in cited publications numbered 6505–6506 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pregnancy Specific Beta–1–glycoprotein 4 (PSG4, Accession NM_002780) is another VGAM1135 host target gene. PSG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PSG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSG4 BINDING SITE, designated SEQ ID:8671, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40984] Another function of VGAM1135 is therefore inhibition of Pregnancy Specific Beta–1–glycoprotein 4 (PSG4, Accession NM_002780), a gene which is a member of the pregnancy–specific glycoprotein (PSG) and CEA families. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSG4. The function of PSG4 has been established by previous studies. The human pregnancy–specific glycoproteins (PSGs) are a group of molecules that

are mainly produced by the placental syncytiotrophoblasts during pregnancy. PSGs comprise a subgroup of the carcinoembryonic antigen (CEA) family, which belongs to the immunoglobulin superfamily. See PSG3 (OMIM Ref. No. 176392) for additional information about PSGs. Teglund et al. (1994) found that the PSG4 gene contains 6 exons. They noted that PSG9, which had been thought to be a novel gene, is in fact an allelic variant of PSG4 that differs by 6 bp in the coding region. (The OMIM Ref. No. 176398.) Studies by several groups resulted in the mapping of the CEA gene family to 19q13.1–q13.2 (Thompson et al., 1990; Thompson et al., 1992; Tynan et al., 1992; Trask et al., 1993). The PSG subgroup is located telomeric of the CEA subgroup, and together they span approximately 1.1 to 1.2 Mb (Brandriff et al., 1992; Tynan et al., 1992). Using a high-resolution restriction fragment fingerprinting technique, Olsen et al. (1994) assembled 256 cosmids spanning the PSG region on 19q13.2 into a single 700-kb contig. FISH to sperm pronuclei and cosmid walking experiments indicated that this PSG contig is telomeric of CGM8 at the telomeric end of the CEA subgroup gene cluster. Detailed restriction mapping and hybridization with gene-specific probes indicated that the order of the

11 PSG genes in the contig is cen--PSG3--PSG8 (OMIM Ref. No. 176397)--PSG12 (PSG10; 176399)--PSG1 (OMIM Ref. No. 176390)--PSG6 (OMIM Ref. No. 176395)--PSG7 (OMIM Ref. No. 176396)--PSG13 (PSG11; 176401)--PSG2 (OMIM Ref. No. 176391)--PSG5 (OMIM Ref. No. 176394)--PSG4--PSG11 (PSG9; 176398)--tel. The PSG genes are tandemly oriented in a 5-prime to 3-prime direction from telomere to centromere. The CEA subgroup gene CGM11 is located at the telomeric end of the PSG gene cluster, and 6 genes belonging to a third CEA family subgroup, namely CGM13 through CGM18 (later OMIM Ref. No. 109770), are interspersed among the PSG genes. Nomenclature: Beauchemin et al. (1999) provided a revised nomenclature for the CEA gene family. Based on this nomenclature, the CEA family is composed of the PSG subfamily, the CEACAM subfamily (see OMIM Ref. No. 109770), and the CEACAM pseudogene (CEACAMP) subfamily (see OMIM Ref. No. 109770). PSG11, PSG12, and PSG13 were renamed PSG9, PSG10, and PSG11, respectively

[40985] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40986] Beauchemin, N.; Draber, P.; Dveksler, G.; Gold, P.; Gray-Owen, S.; Grunert, F.; Hammarstrom, S.; Holmes, K. V.; Karlsson, A.; Kuroki, M.; Lin, S.-H.; Lucka, L.; and 13 others : Redefined nomenclature for members of the carcinoembryonic antigen family. *Exp. Cell Res.* 252: 243-249, 1999. ; and

[40987] Brandriff, B. F.; Gordon, L. A.; Tynan, K. T.; Olsen, A. S.; Mohrenweiser, H. W.; Fertitta, A.; Carrano, A. V.; Trask, B. J. : Order and genomic distances among members of the carcinoem.

[40988] Further studies establishing the function and utilities of PSG4 are found in John Hopkins OMIM database record ID 176393, and in cited publications numbered 2240, 10731, 10742-10740, 1074 and 10744 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pregnancy Specific Beta-1-glycoprotein 7 (PSG7, Accession NM_002783) is another VGAM1135 host target gene. PSG7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSG7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSG7 BINDING SITE,

designated SEQ ID:8672, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40989] Another function of VGAM1135 is therefore inhibition of Pregnancy Specific Beta-1-glycoprotein 7 (PSG7, Accession NM_002783), a gene which function still unknown. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSG7. The function of PSG7 has been established by previous studies. The human pregnancy-specific glycoproteins (PSGs) are a group of molecules that are mainly produced by the placental syncytiotrophoblasts during pregnancy. PSGs comprise a subgroup of the carcinoembryonic antigen (CEA) family, which belongs to the immunoglobulin superfamily. See PSG3 (OMIM Ref. No. 176392) for additional information about PSGs. Teglund et al. (1994) found that the PSG7 gene contains 6 exons. Studies by several groups resulted in the mapping of the CEA gene family to 19q13.1-q13.2 (Thompson et al., 1990; Thompson et al., 1992; Tynan et al., 1992; Trask et al., 1993). The PSG subgroup is located telomeric of the CEA subgroup, and together they span approximately 1.1 to 1.2 Mb (Brandriff et al., 1992; Tynan et al., 1992). Us-

ing a high-resolution restriction fragment fingerprinting technique, Olsen et al. (1994) assembled 256 cosmids spanning the PSG region on 19q13.2 into a single 700-kb contig. FISH to sperm pronuclei and cosmid walking experiments indicated that this PSG contig is telomeric of CGM8 at the telomeric end of the CEA subgroup gene cluster. Detailed restriction mapping and hybridization with gene-specific probes indicated that the order of the 11 PSG genes in the contig is cen--PSG3--PSG8 (OMIM Ref. No. 176397)--PSG12 (PSG10; 176399)--PSG1 (OMIM Ref. No. 176390)--PSG6 (OMIM Ref. No. 176395)--PSG7--PSG13 (PSG11; 176401)--PSG2 (OMIM Ref. No. 176391)--PSG5 (OMIM Ref. No. 176394)--PSG4 (OMIM Ref. No. 176393)--PSG11 (PSG9; 176398)--tel. The PSG genes are tandemly oriented in a 5-prime to 3-prime direction from telomere to centromere. The CEA subgroup gene CGM11 is located at the telomeric end of the PSG gene cluster, and 6 genes belonging to a third CEA family subgroup, namely CGM13 through CGM18 (later OMIM Ref. No. 109770), are interspersed among the PSG genes. Nomenclature: Beauchemin et al. (1999) provided a revised nomenclature for the CEA gene family. Based on this nomenclature, the CEA family is composed

of the PSG subfamily, the CEACAM subfamily (see OMIM Ref. No. 109770), and the CEACAM pseudogene (CEACAMP) subfamily (see OMIM Ref. No. 109770). PSG11, PSG12, and PSG13 were renamed PSG9, PSG10, and PSG11, respectively.

[40990] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[40991] Beauchemin, N.; Draber, P.; Dveksler, G.; Gold, P.; Gray-Owen, S.; Grunert, F.; Hammarstrom, S.; Holmes, K. V.; Karlsson, A.; Kuroki, M.; Lin, S.-H.; Lucka, L.; and 13 others : Redefined nomenclature for members of the carcinoembryonic antigen family. Exp. Cell Res. 252: 243-249, 1999. ; and

[40992] Brandriff, B. F.; Gordon, L. A.; Tynan, K. T.; Olsen, A. S.; Mohrenweiser, H. W.; Fertitta, A.; Carrano, A. V.; Trask, B. J. : Order and genomic distances among members of the carcinoem.

[40993] Further studies establishing the function and utilities of PSG7 are found in John Hopkins OMIM database record ID 176396, and in cited publications numbered 2240, 10731, 10742-10740, 1074 and 10744 listed in the bibliography section hereinbelow, which are also hereby incor-

porated by reference. Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM_003479) is another VGAM1135 host target gene. PTP4A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTP4A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A2 BINDING SITE, designated SEQ ID:9557, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40994] Another function of VGAM1135 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM_003479), a gene which is a protein tyrosine phosphatase which has a C-terminal prenylation site. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A2. The function of PTP4A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. SMURF1 (Accession XM_166483) is another VGAM1135 host target gene. SMURF1 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMURF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMURF1 BINDING SITE, designated SEQ ID:44415, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40995] Another function of VGAM1135 is therefore inhibition of SMURF1 (Accession XM_166483). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMURF1. Syntaxin Binding Protein 1 (STXBP1, Accession NM_003165) is another VGAM1135 host target gene. STXBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STXBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STXBP1 BINDING SITE, designated SEQ ID:9141, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40996] Another function of VGAM1135 is therefore inhibition of Syntaxin Binding Protein 1 (STXBP1, Accession NM_003165), a gene which may play a role in determining the specificity of intracellular fusion reactions. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STXBP1. The function of STXBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM708.SWAP70 (Accession XM_049197) is another VGAM1135 host target gene. SWAP70 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SWAP70, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SWAP70 BINDING SITE, designated SEQ ID:35348, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40997] Another function of VGAM1135 is therefore inhibition of SWAP70 (Accession XM_049197), a gene which is involved not only in nuclear events but also in signaling in B-cell

activation. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SWAP70. The function of SWAP70 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1090. Transcription Factor AP-4 (activating enhancer binding protein 4) (TFAP4, Accession NM_003223) is another VGAM1135 host target gene. TFAP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFAP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFAP4 BINDING SITE, designated SEQ ID:9225, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40998] Another function of VGAM1135 is therefore inhibition of Transcription Factor AP-4 (activating enhancer binding protein 4) (TFAP4, Accession NM_003223), a gene which activates both viral and cellular genes by binding to the symmetrical dna sequence 5'-cagctg-3'. Accordingly, utilities of VGAM1135 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with TFAP4. The function of TFAP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Uncoupling Protein 2 (mitochondrial, proton carrier) (UCP2, Accession NM_003355) is another VGAM1135 host target gene. UCP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by UCP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UCP2 BINDING SITE, designated SEQ ID:9382, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[40999] Another function of VGAM1135 is therefore inhibition of Uncoupling Protein 2 (mitochondrial, proton carrier) (UCP2, Accession NM_003355), a gene which is an inner mitochondrial membrane transporter and uncouples electron transport from oxidative phosphorylation. Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UCP2. The function of UCP2 has been estab-

lished by previous studies. Esterbauer et al. (2001) showed that a common G/A polymorphism in the UCP2 promoter region is associated with enhanced adipose tissue mRNA expression in vivo and results in increased transcription of a reporter gene in the human adipocyte cell line PAZ-6. In analyzing 340 obese and 256 never-obese middle-aged subjects, they found a modest but significant reduction in obesity prevalence associated with the less-common allele. They confirmed this association in a population-based sample of 791 middle-aged subjects from the same geographic area (Salzburg, Austria). Despite its modest effect, but because of its high frequency (approximately 63%), the more-common risk allele conferred a relatively large population-attributable risk accounting for 15% of the obesity in the population studied. Animal model experiments lend further support to the function of UCP2. Zhang et al. (2001) assessed the role of UCP2 in regulating insulin secretion.

Ucp2-deficient mice had higher islet ATP levels and increased glucose-stimulated insulin secretion, establishing that UCP2 negatively regulates insulin secretion. Of pathophysiologic significance, Ucp2 was markedly upregulated in islets of ob/ob mice, a model of obesity-induced

diabetes. Ob/ob mice lacking Ucp2 had restored first-phase insulin secretion, increased serum insulin levels, and greatly decreased levels of glycemia. These results established UCP2 as a key component of beta-cell glucose sensing and as a critical link between obesity, beta-cell dysfunction, and type II diabetes.

[41000] It is appreciated that the abovementioned animal model for UCP2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[41001] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41002] Esterbauer, H.; Schneitler, C.; Oberkofler, H.; Ebenbichler, C.; Paulweber, B.; Sandhofer, F.; Ladurner, G.; Hell, E.; Strosberg, A. D.; Patsch, J. R.; Krempler, F.; Patsch, W. : A common polymorphism in the promoter of UCP2 is associated with decreased risk of obesity in middle-aged humans. *Nature Genet.* 28: 178–183, 2001. ; and

[41003] Zhang, C.-Y.; Baffy, G.; Perret, P.; Krauss, S.; Peroni, O.; Grujic, D.; Hagen, T.; Vidal-Puig, A.; Boss, O.; Kim, Y.-B.; Zheng, X. X.; Wheeler, M. B.; Shulman, G. I.; Chan, C. B.; Lo.

[41004] Further studies establishing the function and utilities of UCP2 are found in John Hopkins OMIM database record ID 601693, and in cited publications numbered 6483–6485, 3700–3701, 6486–6489, 279 and 6707 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. AP1 Gamma Subunit Binding Protein 1 (AP1GBP1, Accession NM_007247) is another VGAM1135 host target gene. AP1GBP1 BINDING SITE1 through AP1GBP1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AP1GBP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1GBP1 BINDING SITE1 through AP1GBP1 BINDING SITE3, designated SEQ ID:14116, SEQ ID:27871 and SEQ ID:27879 respectively, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41005] Another function of VGAM1135 is therefore inhibition of AP1 Gamma Subunit Binding Protein 1 (AP1GBP1, Accession NM_007247). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1GBP1. Chromosome

20 Open Reading Frame 173 (C20orf173, Accession NM_080828) is another VGAM1135 host target gene. C20orf173 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C20orf173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf173 BINDING SITE, designated SEQ ID:28093, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41006] Another function of VGAM1135 is therefore inhibition of Chromosome 20 Open Reading Frame 173 (C20orf173, Accession NM_080828). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf173. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM1135 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

CALN1 BINDING SITE, designated SEQ ID:25513, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41007] Another function of VGAM1135 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Cerebellin 1 Precursor (CBLN1, Accession NM_004352) is another VGAM1135 host target gene. CBLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBLN1 BINDING SITE, designated SEQ ID:10555, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41008] Another function of VGAM1135 is therefore inhibition of Cerebellin 1 Precursor (CBLN1, Accession NM_004352). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBLN1. Calcium Homeostasis Endo-

plasmic Reticulum Protein (CHERP, Accession NM_006387) is another VGAM1135 host target gene. CHERP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHERP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHERP BINDING SITE, designated SEQ ID:13091, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41009] Another function of VGAM1135 is therefore inhibition of Calcium Homeostasis Endoplasmic Reticulum Protein (CHERP, Accession NM_006387). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHERP. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 37 (DDX37, Accession NM_032656) is another VGAM1135 host target gene. DDX37 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX37 BINDING SITE, des-

ignated SEQ ID:26389, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41010] Another function of VGAM1135 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 37 (DDX37, Accession NM_032656). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX37. Dedicator of Cyto-kinesis 3 (DOCK3, Accession XM_039259) is another VGAM1135 host target gene. DOCK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOCK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOCK3 BINDING SITE, designated SEQ ID:33035, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41011] Another function of VGAM1135 is therefore inhibition of Dedicator of Cyto-kinesis 3 (DOCK3, Accession XM_039259). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with DOCK3. EDR2 (Accession XM_018136) is another VGAM1135 host target gene. EDR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDR2 BINDING SITE, designated SEQ ID:30341, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41012] Another function of VGAM1135 is therefore inhibition of EDR2 (Accession XM_018136). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDR2. Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538) is another VGAM1135 host target gene. ERMAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERMAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERMAP BINDING SITE, designated SEQ ID:20609, to the nucleotide sequence of VGAM1135 RNA,

herein designated VGAM RNA, also designated SEQ ID:3846.

[41013] Another function of VGAM1135 is therefore inhibition of Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERMAP. FLJ12681 (Accession NM_022773) is another VGAM1135 host target gene. FLJ12681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12681 BINDING SITE, designated SEQ ID:23037, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41014] Another function of VGAM1135 is therefore inhibition of FLJ12681 (Accession NM_022773). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12681. FLJ12704 (Accession NM_024998) is another VGAM1135 host target gene. FLJ12704 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12704 BINDING SITE, designated SEQ ID:24567, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41015] Another function of VGAM1135 is therefore inhibition of FLJ12704 (Accession NM_024998). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12704. FLJ22501 (Accession NM_024747) is another VGAM1135 host target gene. FLJ22501 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22501 BINDING SITE, designated SEQ ID:24083, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41016] Another function of VGAM1135 is therefore inhibition of

FLJ22501 (Accession NM_024747). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22501. FRAG1 (Accession NM_014489) is another VGAM1135 host target gene. FRAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FRAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRAG1 BINDING SITE, designated SEQ ID:15834, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41017] Another function of VGAM1135 is therefore inhibition of FRAG1 (Accession NM_014489). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FRAG1. HIP-55 (Accession NM_014063) is another VGAM1135 host target gene. HIP-55 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIP-55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of HIP-55 BINDING SITE, designated SEQ ID:15277, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41018] Another function of VGAM1135 is therefore inhibition of HIP-55 (Accession NM_014063). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIP-55. KIAA0552 (Accession NM_014731) is another VGAM1135 host target gene. KIAA0552 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0552, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0552 BINDING SITE, designated SEQ ID:16345, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41019] Another function of VGAM1135 is therefore inhibition of KIAA0552 (Accession NM_014731). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0552. KIAA1193 (Accession XM_041843) is another

VGAM1135 host target gene. KIAA1193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE, designated SEQ ID:33583, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41020] Another function of VGAM1135 is therefore inhibition of KIAA1193 (Accession XM_041843). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. KIAA1196 (Accession XM_028968) is another VGAM1135 host target gene. KIAA1196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1196 BINDING SITE, designated SEQ ID:30822, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41021] Another function of VGAM1135 is therefore inhibition of KIAA1196 (Accession XM_028968). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1196. KIAA1434 (Accession XM_045585) is another VGAM1135 host target gene. KIAA1434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1434 BINDING SITE, designated SEQ ID:34491, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41022] Another function of VGAM1135 is therefore inhibition of KIAA1434 (Accession XM_045585). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1434. KIAA1485 (Accession XM_114619) is another VGAM1135 host target gene. KIAA1485 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1485, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1485 BINDING SITE, designated SEQ ID:43002, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41023] Another function of VGAM1135 is therefore inhibition of KIAA1485 (Accession XM_114619). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1485. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1135 host target gene. LASP1 BINDING SITE1 and LASP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LASP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE1 and LASP1 BINDING SITE2, designated SEQ ID:12796 and SEQ ID:12803 respectively, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41024] Another function of VGAM1135 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148).

Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession NM_017893) is another VGAM1135 host target gene. SEMA4G BINDING SITE1 and SEMA4G BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEMA4G, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4G BINDING SITE1 and SEMA4G BINDING SITE2, designated SEQ ID:19565 and SEQ ID:45416 respectively, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41025] Another function of VGAM1135 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4G (SEMA4G, Accession NM_017893). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4G. Tumor Protein P53 Inducible Nu-

clear Protein 1 (TP53INP1, Accession NM_033285) is another VGAM1135 host target gene. TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TP53INP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2, designated SEQ ID:27110 and SEQ ID:32960 respectively, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41026] Another function of VGAM1135 is therefore inhibition of Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53INP1. LOC113444 (Accession NM_138428) is another VGAM1135 host target gene. LOC113444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC113444 BINDING SITE, designated SEQ ID:28790, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41027] Another function of VGAM1135 is therefore inhibition of LOC113444 (Accession NM_138428). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113444. LOC146733 (Accession XM_097076) is another VGAM1135 host target gene. LOC146733 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146733 BINDING SITE, designated SEQ ID:40732, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41028] Another function of VGAM1135 is therefore inhibition of LOC146733 (Accession XM_097076). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146733. LOC146784 (Accession XM_085588) is an-

other VGAM1135 host target gene. LOC146784 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146784 BINDING SITE, designated SEQ ID:38241, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41029] Another function of VGAM1135 is therefore inhibition of LOC146784 (Accession XM_085588). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146784. LOC148932 (Accession XM_086372) is another VGAM1135 host target gene. LOC148932 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148932 BINDING SITE, designated SEQ ID:38624, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41030] Another function of VGAM1135 is therefore inhibition of LOC148932 (Accession XM_086372). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148932. LOC158263 (Accession XM_088530) is another VGAM1135 host target gene. LOC158263 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158263 BINDING SITE, designated SEQ ID:39801, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41031] Another function of VGAM1135 is therefore inhibition of LOC158263 (Accession XM_088530). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158263. LOC162333 (Accession XM_102591) is another VGAM1135 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42133, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41032] Another function of VGAM1135 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC200830 (Accession XM_117287) is another VGAM1135 host target gene. LOC200830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200830 BINDING SITE, designated SEQ ID:43351, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41033] Another function of VGAM1135 is therefore inhibition of LOC200830 (Accession XM_117287). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC200830. LOC219621 (Accession XM_166148) is another VGAM1135 host target gene. LOC219621 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219621, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219621 BINDING SITE, designated SEQ ID:43969, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41034] Another function of VGAM1135 is therefore inhibition of LOC219621 (Accession XM_166148). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219621. LOC221466 (Accession XM_168087) is another VGAM1135 host target gene. LOC221466 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221466 BINDING SITE, designated SEQ ID:44998, to the nucleotide sequence of VGAM1135 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3846.

[41035] Another function of VGAM1135 is therefore inhibition of LOC221466 (Accession XM_168087). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221466. LOC221833 (Accession XM_166519) is another VGAM1135 host target gene. LOC221833 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221833 BINDING SITE, designated SEQ ID:44456, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41036] Another function of VGAM1135 is therefore inhibition of LOC221833 (Accession XM_166519). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221833. LOC254428 (Accession XM_170932) is another VGAM1135 host target gene. LOC254428 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254428, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254428 BINDING SITE, designated SEQ ID:45719, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41037] Another function of VGAM1135 is therefore inhibition of LOC254428 (Accession XM_170932). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254428. LOC256997 (Accession XM_170900) is another VGAM1135 host target gene. LOC256997 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256997 BINDING SITE, designated SEQ ID:45652, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41038] Another function of VGAM1135 is therefore inhibition of LOC256997 (Accession XM_170900). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC256997. LOC51267 (Accession NM_016511) is another VGAM1135 host target gene. LOC51267 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51267 BINDING SITE, designated SEQ ID:18591, to the nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41039] Another function of VGAM1135 is therefore inhibition of LOC51267 (Accession NM_016511). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51267. LOC59346 (Accession NM_021630) is another VGAM1135 host target gene. LOC59346 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC59346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC59346 BINDING SITE, designated SEQ ID:22272, to the

nucleotide sequence of VGAM1135 RNA, herein designated VGAM RNA, also designated SEQ ID:3846.

[41040] Another function of VGAM1135 is therefore inhibition of LOC59346 (Accession NM_021630). Accordingly, utilities of VGAM1135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC59346. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1136 (VGAM1136) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41041] VGAM1136 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1136 was detected is described hereinabove with reference to Figs. 1–8.

[41042] VGAM1136 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Mild Yellowing Virus. VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41043] VGAM1136 gene encodes a VGAM1136 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1136 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1136 precursor RNA is designated SEQ ID:1122, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1122 is located at position 1677 relative to the genome of Beet Mild Yellowing Virus.

[41044] VGAM1136 precursor RNA folds onto itself, forming VGAM1136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41045] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1136 folded precursor RNA into VGAM1136 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1136 RNA is designated SEQ ID:3847, and is provided hereinbelow with reference to the sequence listing part.

[41046] VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1136 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41047] VGAM1136 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1136 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1136 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41048] The complementary binding of VGAM1136 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1136 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1136 host target RNA into VGAM1136 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41049] It is appreciated that VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1136 host target genes. The mRNA of each one of this plurality of VGAM1136 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1136 RNA, herein designated VGAM RNA, and which when bound by VGAM1136 RNA causes inhibition of translation of respective one or more VGAM1136 host target proteins.

[41050] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1136 gene, herein designated VGAM GENE, on one or more VGAM1136 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[41051] It is yet further appreciated that a function of VGAM1136 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGAM1136 correlate with, and may be deduced from, the identity of the host target genes which VGAM1136 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41052] Nucleotide sequences of the VGAM1136 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1136 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1136 are further described hereinbelow with reference to Table 1.

[41053] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1136 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1136 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41054] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1136 gene, herein designated VGAM is inhibition of expression of VGAM1136 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1136 correlate with, and may be deduced from, the identity of the target genes which VGAM1136 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41055] SORCS2 (Accession NM_020777) is a VGAM1136 host target gene. SORCS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SORCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORCS2 BINDING SITE, designated SEQ ID:21873, to the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, also designated SEQ ID:3847.

[41056] A function of VGAM1136 is therefore inhibition of SORCS2 (Accession NM_020777). Accordingly, utilities of

VGAM1136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORCS2. Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544) is another VGAM1136 host target gene. TAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAP2 BINDING SITE, designated SEQ ID:6140, to the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, also designated SEQ ID:3847.

[41057] Another function of VGAM1136 is therefore inhibition of Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544), a gene which is involved in the transport of antigens from the cytoplasm to a membrane-bound compartment for association with mhc class i molecules. Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAP2. The function of TAP2 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM55. Ras and Rab Interactor 3 (RIN3, Accession NM_024832) is another VGAM1136 host target gene. RIN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RIN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIN3 BINDING SITE, designated SEQ ID:24230, to the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, also designated SEQ ID:3847.

[41058] Another function of VGAM1136 is therefore inhibition of Ras and Rab Interactor 3 (RIN3, Accession NM_024832). Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIN3. LOC145623 (Accession XM_096822) is another VGAM1136 host target gene. LOC145623 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145623 BINDING SITE, desig-

nated SEQ ID:40544, to the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, also designated SEQ ID:3847.

[41059] Another function of VGAM1136 is therefore inhibition of LOC145623 (Accession XM_096822). Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145623. LOC197335 (Accession XM_113866) is another VGAM1136 host target gene. LOC197335 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197335 BINDING SITE, designated SEQ ID:42479, to the nucleotide sequence of VGAM1136 RNA, herein designated VGAM RNA, also designated SEQ ID:3847.

[41060] Another function of VGAM1136 is therefore inhibition of LOC197335 (Accession XM_113866). Accordingly, utilities of VGAM1136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197335. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1137 (VGAM1137) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41061] VGAM1137 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1137 was detected is described hereinabove with reference to Figs. 1–8.

[41062] VGAM1137 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Mild Yellowing Virus. VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41063] VGAM1137 gene encodes a VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1137 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1137 precursor RNA is designated SEQ ID:1123, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1123 is located at position 3269 relative to the

genome of Beet Mild Yellowing Virus.

[41064] VGAM1137 precursor RNA folds onto itself, forming VGAM1137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41065] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1137 folded precursor RNA into VGAM1137 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 89%) nucleotide sequence of VGAM1137 RNA is designated SEQ ID:3848, and is provided hereinbelow with reference to the sequence listing part.

[41066] VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1137 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41067] VGAM1137 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1137 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1137 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41068] The complementary binding of VGAM1137 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1137 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1137 host target RNA into VGAM1137 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41069] It is appreciated that VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1137 host target genes. The mRNA of each one of this plurality of VGAM1137 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1137 RNA, herein designated VGAM RNA, and which when bound by VGAM1137 RNA causes inhibition of translation of respective one or more VGAM1137 host target proteins.

[41070] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1137 gene, herein designated VGAM GENE, on one or more VGAM1137 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41071] It is yet further appreciated that a function of VGAM1137 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1137 include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGAM1137

correlate with, and may be deduced from, the identity of the host target genes which VGAM1137 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41072] Nucleotide sequences of the VGAM1137 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1137 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1137 are further described hereinbelow with reference to Table 1.

[41073] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1137 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1137 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41074] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1137 gene, herein designated VGAM is inhibition of expression of VGAM1137 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1137 correlate with, and may be deduced

from, the identity of the target genes which VGAM1137 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41075] A2BP1 (Accession NM_018723) is a VGAM1137 host target gene. A2BP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by A2BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A2BP1 BINDING SITE, designated SEQ ID:20804, to the nucleotide sequence of VGAM1137 RNA, herein designated VGAM RNA, also designated SEQ ID:3848.

[41076] A function of VGAM1137 is therefore inhibition of A2BP1 (Accession NM_018723). Accordingly, utilities of VGAM1137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A2BP1. NPD009 (Accession XM_170795) is another VGAM1137 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of NPD009 BINDING SITE, designated SEQ ID:45561, to the nucleotide sequence of VGAM1137 RNA, herein designated VGAM RNA, also designated SEQ ID:3848.

[41077] Another function of VGAM1137 is therefore inhibition of NPD009 (Accession XM_170795). Accordingly, utilities of VGAM1137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1138 (VGAM1138) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41078] VGAM1138 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1138 was detected is described hereinabove with reference to Figs. 1–8.

[41079] VGAM1138 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Mild Yellowing Virus. VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[41080] VGAM1138 gene encodes a VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1138 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1138 precursor RNA is designated SEQ ID:1124, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1124 is located at position 1988 relative to the genome of Beet Mild Yellowing Virus.

[41081] VGAM1138 precursor RNA folds onto itself, forming VGAM1138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41082] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1138 folded precursor RNA into VGAM1138 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1138 RNA is designated SEQ ID:3849, and is provided hereinbelow with reference to the sequence listing part.

[41083] VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1138 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41084] VGAM1138 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1138 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1138 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41085] The complementary binding of VGAM1138 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1138 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1138 host target RNA into VGAM1138 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41086] It is appreciated that VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1138 host target genes. The mRNA of each one of this plurality of VGAM1138 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1138 RNA, herein designated VGAM RNA, and which when bound by VGAM1138 RNA causes inhibition of translation of respective one or more VGAM1138 host target proteins.

[41087] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1138 gene, herein designated VGAM GENE, on one or more VGAM1138 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41088] It is yet further appreciated that a function of VGAM1138 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGAM1138 correlate with, and may be deduced from, the identity of the host target genes which VGAM1138 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41089] Nucleotide sequences of the VGAM1138 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1138 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1138 are further described hereinbelow with reference to Table 1.

[41090] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1138 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1138 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41091] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1138 gene, herein designated VGAM is inhibition of expression of VGAM1138 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1138 correlate with, and may be deduced from, the identity of the target genes which VGAM1138 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41092] Adenylate Kinase 1 (AK1, Accession NM_000476) is a VGAM1138 host target gene. AK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK1 BINDING SITE, designated SEQ ID:6085, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41093] A function of VGAM1138 is therefore inhibition of Adenylate Kinase 1 (AK1, Accession NM_000476). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK1. Homeo Box D4 (HOXD4, Accession NM_014621) is another VGAM1138 host target gene. HOXD4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HOXD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD4 BINDING SITE, designated SEQ ID:15978, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41094] Another function of VGAM1138 is therefore inhibition of Homeo Box D4 (HOXD4, Accession NM_014621), a gene which is part of a developmental regulatory system. Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD4. The function of HOXD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM330. Kinase Insert Do-

main Receptor (a type III receptor tyrosine kinase) (KDR, Accession NM_002253) is another VGAM1138 host target gene. KDR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KDR BINDING SITE, designated SEQ ID:8052, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41095] Another function of VGAM1138 is therefore inhibition of Kinase Insert Domain Receptor (a type III receptor tyrosine kinase) (KDR, Accession NM_002253). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KDR. Kruppel-like Factor 8 (KLF8, Accession NM_007250) is another VGAM1138 host target gene. KLF8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KLF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLF8 BINDING SITE, designated SEQ ID:14124, to the nu-

cleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41096] Another function of VGAM1138 is therefore inhibition of Kruppel-like Factor 8 (KLF8, Accession NM_007250). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLF8. MIPOL1 (Accession XM_085077) is another VGAM1138 host target gene. MIPOL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MIPOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIPOL1 BINDING SITE, designated SEQ ID:37813, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41097] Another function of VGAM1138 is therefore inhibition of MIPOL1 (Accession XM_085077). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIPOL1. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558) is another VGAM1138 host target gene. PPP1R8 BINDING SITE1 and

PPP1R8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE1 and PPP1R8 BINDING SITE2, designated SEQ ID:28853 and SEQ ID:8567 respectively, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41098] Another function of VGAM1138 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM101. Periaxin (PRX, Accession NM_020956) is another VGAM1138 host target gene. PRX BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRX BINDING SITE, designated SEQ ID:21937, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41099] Another function of VGAM1138 is therefore inhibition of Periaxin (PRX, Accession NM_020956), a gene which seems to be required for maintenance of peripheral nerve myelin sheath. may have a role in axon–glial interactions, possibly by interacting with the cytoplasmic domains of integral membrane proteins such as myelin–associated glycoprotein in the periaxonal regions of the schwann cell plasma membrane. may have a role in the early phases of myelin deposition. Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRX. The function of PRX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM476.SAR1 (Accession NM_020150) is another VGAM1138 host target gene. SAR1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by SAR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAR1 BINDING SITE, designated SEQ ID:21351, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41100] Another function of VGAM1138 is therefore inhibition of SAR1 (Accession NM_020150), a gene which is involved in transport from the endoplasmic reticulum to the golgi apparatus (by similarity). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAR1. The function of SAR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM222.Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM1138 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28439, SEQ ID:28456 and SEQ ID:17175 respectively, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41101] Another function of VGAM1138 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.C6.1A (Accession NM_024332) is another VGAM1138 host target gene. C6.1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6.1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6.1A BINDING SITE, designated SEQ ID:23638, to the nucleotide sequence of

VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41102] Another function of VGAM1138 is therefore inhibition of C6.1A (Accession NM_024332). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6.1A. CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM_003672) is another VGAM1138 host target gene. CDC14A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC14A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14A BINDING SITE, designated SEQ ID:9765, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41103] Another function of VGAM1138 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM_003672). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14A. CCR4-NOT Transcription Complex, Subunit 7

(CNOT7, Accession NM_013354) is another VGAM1138 host target gene. CNOT7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNOT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT7 BINDING SITE, designated SEQ ID:15002, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41104] Another function of VGAM1138 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 7 (CNOT7, Accession NM_013354). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT7. DKFZP434J193 (Accession XM_048452) is another VGAM1138 host target gene. DKFZP434J193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434J193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J193 BINDING SITE, designated SEQ ID:35166, to

the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41105] Another function of VGAM1138 is therefore inhibition of DKFZP434J193 (Accession XM_048452). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J193. DKFZp761H2121 (Accession NM_138339) is another VGAM1138 host target gene. DKFZp761H2121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761H2121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761H2121 BINDING SITE, designated SEQ ID:28738, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41106] Another function of VGAM1138 is therefore inhibition of DKFZp761H2121 (Accession NM_138339). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761H2121. FLJ10716 (Accession NM_018191) is another VGAM1138 host target gene. FLJ10716 BIND-

ING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10716 BINDING SITE, designated SEQ ID:20044, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41107] Another function of VGAM1138 is therefore inhibition of FLJ10716 (Accession NM_018191). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10716. FLJ10738 (Accession NM_018199) is another VGAM1138 host target gene. FLJ10738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10738 BINDING SITE, designated SEQ ID:20068, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41108] Another function of VGAM1138 is therefore inhibition of

FLJ10738 (Accession NM_018199). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10738. FLJ22301 (Accession NM_024836) is another VGAM1138 host target gene. FLJ22301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22301 BINDING SITE, designated SEQ ID:24241, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41109] Another function of VGAM1138 is therefore inhibition of FLJ22301 (Accession NM_024836). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22301. KIAA0182 (Accession XM_050495) is another VGAM1138 host target gene. KIAA0182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0182 BINDING SITE, designated SEQ ID:35642, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41110] Another function of VGAM1138 is therefore inhibition of KIAA0182 (Accession XM_050495). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0182. KIAA0494 (Accession NM_014774) is another VGAM1138 host target gene. KIAA0494 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0494 BINDING SITE, designated SEQ ID:16586, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41111] Another function of VGAM1138 is therefore inhibition of KIAA0494 (Accession NM_014774). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0494. KIAA0660 (Accession NM_012297) is another

VGAM1138 host target gene. KIAA0660 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0660, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0660 BINDING SITE, designated SEQ ID:14656, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41112] Another function of VGAM1138 is therefore inhibition of KIAA0660 (Accession NM_012297). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0660. RNF9 (Accession NM_052828) is another VGAM1138 host target gene. RNF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF9 BINDING SITE, designated SEQ ID:27410, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41113] Another function of VGAM1138 is therefore inhibition of RNF9 (Accession NM_052828). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF9. LOC124222 (Accession XM_058784) is another VGAM1138 host target gene. LOC124222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124222 BINDING SITE, designated SEQ ID:36741, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41114] Another function of VGAM1138 is therefore inhibition of LOC131870 (Accession XM_059544). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131870. LOC131870 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131870, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131870 BINDING SITE, designated SEQ ID:37017, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41115] Another function of VGAM1138 is therefore inhibition of LOC131870 (Accession XM_059544). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131870. LOC150213 (Accession XM_059324) is another VGAM1138 host target gene. LOC150213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150213 BINDING SITE, designated SEQ ID:36959, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41116] Another function of VGAM1138 is therefore inhibition of LOC150213 (Accession XM_059324). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150213. LOC150236 (Accession XM_086824) is another VGAM1138 host target gene. LOC150236 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150236 BINDING SITE, designated SEQ ID:38905, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41117] Another function of VGAM1138 is therefore inhibition of LOC150236 (Accession XM_086824). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150236. LOC220840 (Accession XM_165514) is another VGAM1138 host target gene. LOC220840 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220840, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220840 BINDING SITE, designated SEQ ID:43658, to the nucleotide sequence of VGAM1138 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3849.

[41118] Another function of VGAM1138 is therefore inhibition of LOC220840 (Accession XM_165514). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220840. LOC221914 (Accession XM_168232) is another VGAM1138 host target gene. LOC221914 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221914 BINDING SITE, designated SEQ ID:45099, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41119] Another function of VGAM1138 is therefore inhibition of LOC221914 (Accession XM_168232). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221914. LOC257277 (Accession XM_170867) is another VGAM1138 host target gene. LOC257277 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257277, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257277 BINDING SITE, designated SEQ ID:45640, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41120] Another function of VGAM1138 is therefore inhibition of LOC257277 (Accession XM_170867). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257277. LOC91464 (Accession XM_038589) is another VGAM1138 host target gene. LOC91464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91464 BINDING SITE, designated SEQ ID:32872, to the nucleotide sequence of VGAM1138 RNA, herein designated VGAM RNA, also designated SEQ ID:3849.

[41121] Another function of VGAM1138 is therefore inhibition of LOC91464 (Accession XM_038589). Accordingly, utilities of VGAM1138 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1139 (VGAM1139) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41122] VGAM1139 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1139 was detected is described hereinabove with reference to Figs. 1–8.

[41123] VGAM1139 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote Mosaic Tymovirus. VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41124] VGAM1139 gene encodes a VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1139 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1139 precursor RNA is desig-

nated SEQ ID:1125, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1125 is located at position 4987 relative to the genome of Chayote Mosaic Tymovirus.

- [41125] VGAM1139 precursor RNA folds onto itself, forming VGAM1139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41126] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1139 folded precursor RNA into VGAM1139 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 88%) nucleotide sequence of VGAM1139 RNA is designated SEQ ID:3850, and is provided hereinbelow with reference to the sequence

listing part.

[41127] VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1139 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41128] VGAM1139 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1139 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1139 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41129] The complementary binding of VGAM1139 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1139 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1139 host target RNA into VGAM1139 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41130] It is appreciated that VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1139 host target genes. The mRNA of each one of this plurality of VGAM1139 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1139 RNA, herein designated VGAM

RNA, and which when bound by VGAM1139 RNA causes inhibition of translation of respective one or more VGAM1139 host target proteins.

[41131] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1139 gene, herein designated VGAM GENE, on one or more VGAM1139 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41132] It is yet further appreciated that a function of VGAM1139 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1139 include diagnosis, prevention and treatment of viral infection by Chayote Mosaic Tymovirus. Specific functions, and accordingly utilities, of VGAM1139 correlate with, and may be deduced from, the identity of the host target genes which VGAM1139 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41133] Nucleotide sequences of the VGAM1139 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1139 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1139 are further described hereinbelow with reference to Table 1.

[41134] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1139 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1139 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41135] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1139 gene, herein designated VGAM is

inhibition of expression of VGAM1139 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1139 correlate with, and may be deduced from, the identity of the target genes which VGAM1139 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41136] Chromosome 20 Open Reading Frame 36 (C20orf36, Accession NM_018257) is a VGAM1139 host target gene. C20orf36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf36 BINDING SITE, designated SEQ ID:20221, to the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, also designated SEQ ID:3850.

[41137] A function of VGAM1139 is therefore inhibition of Chromosome 20 Open Reading Frame 36 (C20orf36, Accession NM_018257). Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf36. DKFZp586I021 (Accession NM_032271) is another VGAM1139 host target

gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26027, to the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, also designated SEQ ID:3850.

[41138] Another function of VGAM1139 is therefore inhibition of DKFZp586I021 (Accession NM_032271). Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. LOC154834 (Accession XM_098621) is another VGAM1139 host target gene. LOC154834 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154834, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154834 BINDING SITE, designated SEQ ID:41732, to the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, also designated SEQ

ID:3850.

[41139] Another function of VGAM1139 is therefore inhibition of LOC154834 (Accession XM_098621). Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154834. LOC169026 (Accession XM_095471) is another VGAM1139 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40261, to the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, also designated SEQ ID:3850.

[41140] Another function of VGAM1139 is therefore inhibition of LOC169026 (Accession XM_095471). Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. LOC201292 (Accession XM_113949) is another VGAM1139 host target gene. LOC201292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201292, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201292 BINDING SITE, designated SEQ ID:42563, to the nucleotide sequence of VGAM1139 RNA, herein designated VGAM RNA, also designated SEQ ID:3850.

[41141] Another function of VGAM1139 is therefore inhibition of LOC201292 (Accession XM_113949). Accordingly, utilities of VGAM1139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201292. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1140 (VGAM1140) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41142] VGAM1140 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1140 was detected is described hereinabove with reference to Figs. 1-8.

[41143] VGAM1140 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote Mosaic Ty-

movirus. VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41144] VGAM1140 gene encodes a VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1140 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1140 precursor RNA is designated SEQ ID:1126, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1126 is located at position 709 relative to the genome of Chayote Mosaic Tymovirus.

[41145] VGAM1140 precursor RNA folds onto itself, forming VGAM1140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41146] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1140 folded precursor RNA into VGAM1140 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1140 RNA is designated SEQ ID:3851, and is provided hereinbelow with reference to the sequence listing part.

[41147] VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1140 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41148] VGAM1140 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1140 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1140 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41149] The complementary binding of VGAM1140 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1140 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1140 host target RNA into VGAM1140 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41150] It is appreciated that VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1140 host target genes. The mRNA of each one of this plurality of VGAM1140 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1140 RNA, herein designated VGAM RNA, and which when bound by VGAM1140 RNA causes inhibition of translation of respective one or more VGAM1140 host target proteins.

[41151] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1140 gene, herein designated VGAM GENE, on one or more VGAM1140 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41152] It is yet further appreciated that a function of VGAM1140 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1140 include diagnosis, prevention and treatment of viral infection by Chayote Mosaic Tymovirus. Specific functions, and accordingly utilities, of VGAM1140 correlate with, and may be deduced from, the identity of the host target genes which VGAM1140 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41153] Nucleotide sequences of the VGAM1140 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1140 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1140 are further described hereinbelow with reference to Table 1.

[41154] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1140 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1140 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41155] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1140 gene, herein designated VGAM is inhibition of expression of VGAM1140 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1140 correlate with, and may be deduced from, the identity of the target genes which VGAM1140 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41156] ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028) is a VGAM1140 host target gene. ATP11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11A BINDING SITE, designated SEQ ID:37800, to the

nucleotide sequence of VGAM1140 RNA, herein designated VGAM RNA, also designated SEQ ID:3851.

[41157] A function of VGAM1140 is therefore inhibition of ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028). Accordingly, utilities of VGAM1140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11A. FLJ22056 (Accession NM_022489) is another VGAM1140 host target gene. FLJ22056 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22056 BINDING SITE, designated SEQ ID:22868, to the nucleotide sequence of VGAM1140 RNA, herein designated VGAM RNA, also designated SEQ ID:3851.

[41158] Another function of VGAM1140 is therefore inhibition of FLJ22056 (Accession NM_022489). Accordingly, utilities of VGAM1140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22056. LOC253461 (Accession XM_172341) is another VGAM1140 host target gene. LOC253461 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253461 BINDING SITE, designated SEQ ID:46073, to the nucleotide sequence of VGAM1140 RNA, herein designated VGAM RNA, also designated SEQ ID:3851.

[41159] Another function of VGAM1140 is therefore inhibition of LOC253461 (Accession XM_172341). Accordingly, utilities of VGAM1140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253461. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1141 (VGAM1141) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41160] VGAM1141 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1141 was detected is described hereinabove with reference to Figs. 1-8.

[41161] VGAM1141 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Chayote Mosaic Ty-movirus. VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41162] VGAM1141 gene encodes a VGAM1141 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1141 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1141 precursor RNA is designated SEQ ID:1127, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1127 is located at position 1116 relative to the genome of Chayote Mosaic Tymovirus.

[41163] VGAM1141 precursor RNA folds onto itself, forming VGAM1141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[41164] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1141 folded precursor RNA into VGAM1141 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1141 RNA is designated SEQ ID:3852, and is provided hereinbelow with reference to the sequence listing part.

[41165] VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1141 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41166] VGAM1141 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1141 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1141 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1141 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41167] The complementary binding of VGAM1141 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1141 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1141 host target RNA into VGAM1141 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41168] It is appreciated that VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1141 host target genes. The mRNA of each one of this plurality of VGAM1141 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1141 RNA, herein designated VGAM RNA, and which when bound by VGAM1141 RNA causes inhibition of translation of respective one or more VGAM1141 host target proteins.

[41169] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1141 gene, herein designated VGAM GENE, on one or more VGAM1141 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41170] It is yet further appreciated that a function of VGAM1141 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1141 include diagnosis, prevention and treatment of viral infection by Chayote Mosaic Tymovirus. Specific functions, and accordingly utilities, of VGAM1141 correlate with, and may be deduced from, the identity of the host target genes which VGAM1141 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41171] Nucleotide sequences of the VGAM1141 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1141 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1141 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1141 are further described hereinbelow with reference to Table 1.

[41172] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1141 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1141 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41173] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1141 gene, herein designated VGAM is inhibition of expression of VGAM1141 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1141 correlate with, and may be deduced from, the identity of the target genes which VGAM1141 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41174] Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621) is a VGAM1141 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10975, to the nucleotide sequence of VGAM1141 RNA, herein designated VGAM RNA, also designated SEQ ID:3852.

[41175] A function of VGAM1141 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM1141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. NTT73 (Accession NM_018057) is another VGAM1141 host target gene. NTT73 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTT73, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTT73 BINDING SITE, designated SEQ ID:19820, to the nucleotide sequence of VGAM1141 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3852.

[41176] Another function of VGAM1141 is therefore inhibition of NTT73 (Accession NM_018057). Accordingly, utilities of VGAM1141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTT73. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1142 (VGAM1142) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41177] VGAM1142 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1142 was detected is described hereinabove with reference to Figs. 1–8.

[41178] VGAM1142 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bamboo Mosaic Virus. VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41179] VGAM1142 gene encodes a VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1142 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1142 precursor RNA is designated SEQ ID:1128, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1128 is located at position 5891 relative to the genome of Bamboo Mosaic Virus.

- [41180] VGAM1142 precursor RNA folds onto itself, forming VGAM1142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41181] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1142 folded precursor RNA into VGAM1142 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1142 RNA is designated SEQ ID:3853, and is provided hereinbelow with reference to the sequence listing part.

[41182] VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1142 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[41183] VGAM1142 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1142 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1142 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41184] The complementary binding of VGAM1142 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1142 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1142 host target RNA into VGAM1142 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41185] It is appreciated that VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1142 host target genes. The mRNA of each one of this plurality of VGAM1142 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1142 RNA, herein designated VGAM RNA, and which when bound by VGAM1142 RNA causes inhibition of translation of respective one or more VGAM1142 host target proteins.

[41186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1142 gene, herein designated VGAM GENE, on one or more VGAM1142 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41187] It is yet further appreciated that a function of VGAM1142 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of viral infection by Bamboo Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1142 correlate with, and may be deduced from, the identity of the host target genes which VGAM1142 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41188] Nucleotide sequences of the VGAM1142 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1142 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1142 are further described hereinbelow with reference to Table 1.

[41189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1142 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1142 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[41190] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1142 gene, herein designated VGAM is inhibition of expression of VGAM1142 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1142 correlate with, and may be deduced from, the identity of the target genes which VGAM1142 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41191] LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055) is a VGAM1142 host target gene. LANCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANCL1 BINDING SITE, designated SEQ ID:12692, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41192] A function of VGAM1142 is therefore inhibition of LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055), a gene which binds the

C-terminus of stomatin. Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANCL1. The function of LANCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM656. Protocadherin 9 (PCDH9, Accession XM_096054) is another VGAM1142 host target gene. PCDH9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCDH9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH9 BINDING SITE, designated SEQ ID:40294, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41193] Another function of VGAM1142 is therefore inhibition of Protocadherin 9 (PCDH9, Accession XM_096054). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH9. Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449) is an-

other VGAM1142 host target gene. RFX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6048, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41194] Another function of VGAM1142 is therefore inhibition of Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449), a gene which activates transcription from class ii mhc promoters. Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177) is another VGAM1142 host target gene. C17orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf26, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf26 BINDING SITE, designated SEQ ID:29183, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41195] Another function of VGAM1142 is therefore inhibition of Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf26. Calcium-binding tyrosine-(Y)-phosphorylation Regulated (fibrousheathin 2) (CABYR, Accession NM_012189) is another VGAM1142 host target gene. CABYR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CABYR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CABYR BINDING SITE, designated SEQ ID:14476, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41196] Another function of VGAM1142 is therefore inhibition of

Calcium-binding tyrosine-(Y)-phosphorylation Regulated (fibrousheathin 2) (CABYR, Accession NM_012189). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CABYR. FLJ10579 (Accession NM_018145) is another VGAM1142 host target gene. FLJ10579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10579 BINDING SITE, designated SEQ ID:19944, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41197] Another function of VGAM1142 is therefore inhibition of FLJ10579 (Accession NM_018145). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10579. FLJ11618 (Accession NM_022452) is another VGAM1142 host target gene. FLJ11618 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11618 BINDING SITE, designated SEQ ID:22790, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41198] Another function of VGAM1142 is therefore inhibition of FLJ11618 (Accession NM_022452). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11618. Huntingtin-associated Protein Interacting Protein (duo) (HAPIP, Accession NM_003947) is another VGAM1142 host target gene. HAPIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAPIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAPIP BINDING SITE, designated SEQ ID:10066, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41199] Another function of VGAM1142 is therefore inhibition of Huntingtin-associated Protein Interacting Protein (duo) (HAPIP, Accession NM_003947). Accordingly, utilities of

VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAPIP. KIAA0515 (Accession XM_033380) is another VGAM1142 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31915, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41200] Another function of VGAM1142 is therefore inhibition of KIAA0515 (Accession XM_033380). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. NPD009 (Accession XM_170795) is another VGAM1142 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPD009

BINDING SITE, designated SEQ ID:45559, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41201] Another function of VGAM1142 is therefore inhibition of NPD009 (Accession XM_170795). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Pellino Homolog 2 (Drosophila) (PELI2, Accession NM_021255) is another VGAM1142 host target gene. PELI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PELI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI2 BINDING SITE, designated SEQ ID:22227, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41202] Another function of VGAM1142 is therefore inhibition of Pellino Homolog 2 (Drosophila) (PELI2, Accession NM_021255). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI2. LOC116411 (Accession XM_058095) is another VGAM1142 host target

gene. LOC116411 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC116411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116411 BINDING SITE, designated SEQ ID:36563, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41203] Another function of VGAM1142 is therefore inhibition of LOC116411 (Accession XM_058095). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116411. LOC51094 (Accession NM_015999) is another VGAM1142 host target gene. LOC51094 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51094, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51094 BINDING SITE, designated SEQ ID:18088, to the nucleotide sequence of VGAM1142 RNA, herein designated VGAM RNA, also designated SEQ ID:3853.

[41204] Another function of VGAM1142 is therefore inhibition of LOC51094 (Accession NM_015999). Accordingly, utilities of VGAM1142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51094. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1143 (VGAM1143) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41205] VGAM1143 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1143 was detected is described hereinabove with reference to Figs. 1–8.

[41206] VGAM1143 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bamboo Mosaic Virus. VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41207] VGAM1143 gene encodes a VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1143 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1143 precursor RNA is designated SEQ ID:1129, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1129 is located at position 1369 relative to the genome of Bamboo Mosaic Virus.

[41208] VGAM1143 precursor RNA folds onto itself, forming VGAM1143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41209] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1143 folded precursor RNA into VGAM1143 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1143 RNA is designated SEQ ID:3854, and is provided hereinbelow with reference to the sequence listing part.

[41210] VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1143 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41211] VGAM1143 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1143 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1143 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41212] The complementary binding of VGAM1143 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1143 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1143 host target RNA into VGAM1143 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41213] It is appreciated that VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1143 host target genes. The mRNA of each one of this plurality of VGAM1143 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1143 RNA, herein designated VGAM RNA, and which when bound by VGAM1143 RNA causes inhibition of translation of respective one or more VGAM1143 host target proteins.

[41214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1143 gene, herein designated VGAM GENE, on one or more VGAM1143 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41215] It is yet further appreciated that a function of VGAM1143 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1143 include diagnosis, prevention and treatment of viral infection by Bamboo Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1143 correlate with, and may be deduced from, the identity of the host target genes which VGAM1143 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41216] Nucleotide sequences of the VGAM1143 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1143 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1143 are further described hereinbelow with reference to Table 1.

[41217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1143 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1143 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[41218] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1143 gene, herein designated VGAM is inhibition of expression of VGAM1143 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1143 correlate with, and may be deduced from, the identity of the target genes which VGAM1143 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41219] Extracellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM_001393) is a VGAM1143 host target gene. ECM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ECM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ECM2 BINDING SITE, designated SEQ ID:7085, to the nucleotide sequence of VGAM1143 RNA, herein designated VGAM RNA, also designated SEQ ID:3854.

[41220] A function of VGAM1143 is therefore inhibition of Extracellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM_001393). Accordingly, utili-

ties of VGAM1143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ECM2. G Protein-coupled Receptor, Family C, Group 5, Member B (GPRC5B, Accession NM_016235) is another VGAM1143 host target gene. GPRC5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPRC5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRC5B BINDING SITE, designated SEQ ID:18348, to the nucleotide sequence of VGAM1143 RNA, herein designated VGAM RNA, also designated SEQ ID:3854.

[41221] Another function of VGAM1143 is therefore inhibition of G Protein-coupled Receptor, Family C, Group 5, Member B (GPRC5B, Accession NM_016235), a gene which belongs to G protein-coupled receptor. Accordingly, utilities of VGAM1143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRC5B. The function of GPRC5B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Leukocyte Immunoglobulin-like

Receptor, Subfamily B (with TM and ITIM domains), Member 4 (LILRB4, Accession NM_006847) is another VGAM1143 host target gene. LILRB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LILRB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LILRB4 BINDING SITE, designated SEQ ID:13716, to the nucleotide sequence of VGAM1143 RNA, herein designated VGAM RNA, also designated SEQ ID:3854.

[41222] Another function of VGAM1143 is therefore inhibition of Leukocyte Immunoglobulin-like Receptor, Subfamily B (with TM and ITIM domains), Member 4 (LILRB4, Accession NM_006847). Accordingly, utilities of VGAM1143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LILRB4. KIAA1161 (Accession XM_088501) is another VGAM1143 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39749, to the nucleotide sequence of VGAM1143 RNA, herein designated VGAM RNA, also designated SEQ ID:3854.

[41223] Another function of VGAM1143 is therefore inhibition of KIAA1161 (Accession XM_088501). Accordingly, utilities of VGAM1143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1144 (VGAM1144) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41224] VGAM1144 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1144 was detected is described hereinabove with reference to Figs. 1–8.

[41225] VGAM1144 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bamboo Mosaic Virus. VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[41226] VGAM1144 gene encodes a VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1144 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1144 precursor RNA is designated SEQ ID:1130, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1130 is located at position 502 relative to the genome of Bamboo Mosaic Virus.

[41227] VGAM1144 precursor RNA folds onto itself, forming VGAM1144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41228] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1144 folded precursor RNA into VGAM1144 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1144 RNA is designated SEQ ID:3855, and is provided hereinbelow with reference to the sequence listing part.

[41229] VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1144 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41230] VGAM1144 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1144 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1144 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41231] The complementary binding of VGAM1144 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1144 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1144 host target RNA into VGAM1144 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41232] It is appreciated that VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1144 host target genes. The mRNA of each one of this plurality of VGAM1144 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1144 RNA, herein designated VGAM RNA, and which when bound by VGAM1144 RNA causes inhibition of translation of respective one or more VGAM1144 host target proteins.

[41233] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1144 gene, herein designated VGAM GENE, on one or more VGAM1144 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41234] It is yet further appreciated that a function of VGAM1144 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of viral infection by Bamboo Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1144 correlate with, and may be deduced from, the identity of the host target genes which VGAM1144 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41235] Nucleotide sequences of the VGAM1144 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1144 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1144 are further described hereinbelow with reference to Table 1.

[41236] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1144 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1144 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41237] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1144 gene, herein designated VGAM is inhibition of expression of VGAM1144 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1144 correlate with, and may be deduced from, the identity of the target genes which VGAM1144 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41238] Cyclin F (CCNF, Accession NM_001761) is a VGAM1144 host target gene. CCNF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNF BINDING SITE, designated SEQ ID:7522, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41239] A function of VGAM1144 is therefore inhibition of Cyclin F (CCNF, Accession NM_001761), a gene which likely to be involved in the control of the cell cycle during s phase and g2. Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNF. The function of CCNF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM367. TAF7-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 50kDa (TAF7L, Accession NM_024885) is another VGAM1144 host target gene. TAF7L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAF7L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF7L BINDING SITE, designated SEQ ID:24339, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41240] Another function of VGAM1144 is therefore inhibition of TAF7-like RNA Polymerase II, TATA Box Binding Protein (TBP)-associated Factor, 50kDa (TAF7L, Accession

NM_024885). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF7L. Fer-1-like 4 (C. elegans) (FER1L4, Accession NM_025206) is another VGAM1144 host target gene. FER1L4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FER1L4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FER1L4 BINDING SITE, designated SEQ ID:24871, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41241] Another function of VGAM1144 is therefore inhibition of Fer-1-like 4 (C. elegans) (FER1L4, Accession NM_025206). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FER1L4. KIAA0040 (Accession NM_014656) is another VGAM1144 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16094, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41242] Another function of VGAM1144 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. LHX6 (Accession NM_014368) is another VGAM1144 host target gene. LHX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LHX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHX6 BINDING SITE, designated SEQ ID:15697, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41243] Another function of VGAM1144 is therefore inhibition of LHX6 (Accession NM_014368). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHX6.

LOC160414 (Accession XM_100898) is another VGAM1144 host target gene. LOC160414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC160414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160414 BINDING SITE, designated SEQ ID:42106, to the nucleotide sequence of VGAM1144 RNA, herein designated VGAM RNA, also designated SEQ ID:3855.

[41244] Another function of VGAM1144 is therefore inhibition of LOC160414 (Accession XM_100898). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160414. LOC51716 (Accession NM_016280) is another VGAM1144 host target gene. LOC51716 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51716 BINDING SITE, designated SEQ ID:18403, to the nucleotide sequence of VGAM1144 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3855.

[41245] Another function of VGAM1144 is therefore inhibition of LOC51716 (Accession NM_016280). Accordingly, utilities of VGAM1144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51716. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1145 (VGAM1145) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41246] VGAM1145 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1145 was detected is described hereinabove with reference to Figs. 1–8.

[41247] VGAM1145 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bamboo Mosaic Virus. VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41248] VGAM1145 gene encodes a VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1145 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1145 precursor RNA is designated SEQ ID:1131, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1131 is located at position 5368 relative to the genome of Bamboo Mosaic Virus.

- [41249] VGAM1145 precursor RNA folds onto itself, forming VGAM1145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41250] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1145 folded precursor RNA into VGAM1145 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1145 RNA is designated SEQ ID:3856, and is provided hereinbelow with reference to the sequence listing part.

[41251] VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1145 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41252] VGAM1145 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1145 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1145 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[41253] The complementary binding of VGAM1145 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1145 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1145 host target RNA into VGAM1145 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41254] It is appreciated that VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1145 host target genes. The mRNA of

each one of this plurality of VGAM1145 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1145 RNA, herein designated VGAM RNA, and which when bound by VGAM1145 RNA causes inhibition of translation of respective one or more VGAM1145 host target proteins.

[41255] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1145 gene, herein designated VGAM GENE, on one or more VGAM1145 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[41256] It is yet further appreciated that a function of VGAM1145 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of viral infection by Bamboo Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1145 correlate with, and may be deduced from, the identity of the host target genes which VGAM1145 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41257] Nucleotide sequences of the VGAM1145 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1145 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1145 are further described hereinbelow with reference to Table 1.

[41258] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1145 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1145 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41259] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1145 gene, herein designated VGAM is inhibition of expression of VGAM1145 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1145 correlate with, and may be deduced from, the identity of the target genes which VGAM1145 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41260] UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 7 (B3GNT7, Accession XM_048735) is a VGAM1145 host target gene. B3GNT7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B3GNT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT7 BINDING SITE, designated SEQ ID:35238, to the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, also designated SEQ ID:3856.

[41261] A function of VGAM1145 is therefore inhibition of UDP-

GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 7 (B3GNT7, Accession XM_048735). Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT7. Carbohydrate (N-acetylglucosamine 6-O) Sulfo-transferase 4 (CHST4, Accession NM_005769) is another VGAM1145 host target gene. CHST4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST4 BINDING SITE, designated SEQ ID:12338, to the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, also designated SEQ ID:3856.

[41262] Another function of VGAM1145 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769). Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST4. Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943) is another VGAM1145 host target gene. CLIC4 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by CLIC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC4 BINDING SITE, designated SEQ ID:15128, to the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, also designated SEQ ID:3856.

[41263] Another function of VGAM1145 is therefore inhibition of Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943). Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC4. FLJ11274 (Accession NM_018375) is another VGAM1145 host target gene. FLJ11274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11274 BINDING SITE, designated SEQ ID:20398, to the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, also designated SEQ ID:3856.

[41264] Another function of VGAM1145 is therefore inhibition of

FLJ11274 (Accession NM_018375). Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11274. FLJ12903 (Accession NM_022753) is another VGAM1145 host target gene. FLJ12903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12903 BINDING SITE, designated SEQ ID:22976, to the nucleotide sequence of VGAM1145 RNA, herein designated VGAM RNA, also designated SEQ ID:3856.

[41265] Another function of VGAM1145 is therefore inhibition of FLJ12903 (Accession NM_022753). Accordingly, utilities of VGAM1145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12903. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1146 (VGAM1146) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[41266] VGAM1146 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1146 was detected is described hereinabove with reference to Figs. 1–8.

[41267] VGAM1146 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41268] VGAM1146 gene encodes a VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1146 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1146 precursor RNA is designated SEQ ID:1132, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1132 is located at position 218150 relative to the genome of Fowlpox Virus.

[41269] VGAM1146 precursor RNA folds onto itself, forming VGAM1146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41270] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1146 folded precursor RNA into VGAM1146 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1146 RNA is designated SEQ ID:3857, and is provided hereinbelow with reference to the sequence listing part.

[41271] VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1146 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[41272] VGAM1146 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1146 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1146 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[41273] The complementary binding of VGAM1146 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1146 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1146 host target RNA into VGAM1146 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41274] It is appreciated that VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1146 host target genes. The mRNA of each one of this plurality of VGAM1146 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1146 RNA, herein designated VGAM RNA, and which when bound by VGAM1146 RNA causes inhibition of translation of respective one or more VGAM1146 host target proteins.

[41275] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1146 gene, herein designated VGAM GENE, on one

or more VGAM1146 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41276] It is yet further appreciated that a function of VGAM1146 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1146 correlate with, and may be deduced from, the identity of the host target genes which VGAM1146 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41277] Nucleotide sequences of the VGAM1146 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1146 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1146 are further described hereinbelow with reference to Table 1.

[41278] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1146 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1146 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41279] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1146 gene, herein designated VGAM is inhibition of expression of VGAM1146 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1146 correlate with, and may be deduced from, the identity of the target genes which VGAM1146 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41280] ACT (Accession NM_020482) is a VGAM1146 host target

gene. ACT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACT BINDING SITE, designated SEQ ID:21735, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41281] A function of VGAM1146 is therefore inhibition of ACT (Accession NM_020482), a gene which a plasma protease inhibitor synthesized in the liver. Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACT. The function of ACT has been established by previous studies. Alpha-1-antichymotrypsin is a plasma protease inhibitor synthesized in the liver. It is a single glycopeptide chain of about 68,000 daltons and belongs to the class of serine protease inhibitors. In man, the normal serum level is about one-tenth that of alpha-1-antitrypsin (PI; 107400), with which it shares nucleic acid and protein sequence homology (Chandra et al., 1983). Both are major acute phase reactants; their concentrations in plasma increase in response to trauma, surgery, and infection. An-

tithrombin III, which also is structurally similar to alpha-1-antitrypsin, shows less sequence homology to antichymotrypsin and is not an acute phase reactant. Sefton et al. (1990) concluded that the PI-PIL gene cluster is only 220 kb away from the AACT gene and that it is oriented in the opposite direction. (PIL refers to 'PI-like' and is also referred to as 'antitrypsin-related,' or ATR (OMIM Ref. No. 107410).) The comparatively short interval between the genes came as a surprise given previous estimates of the level of genetic recombination between them. By PCR-single strand conformation polymorphism (SSCP) analysis, Tsuda et al. (1992) identified a point mutation in exon 5 of the AACT gene resulting in substitution of met by val at codon 389. The mutation, an A-to-G transition at base-pair 1252, was found in heterozygous state in 6 patients; 4 of the 6 (aged 38, 43, 69, and 80 years) had occlusive cerebrovascular disease.

[41282] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41283] Chandra, T.; Stackhouse, R.; Kidd, V. J.; Robson, K. J. H.; Woo, S. L. C. : Sequence homology between human alpha-1-antichymotrypsin, alpha-1-antitrypsin, and antithrom-

bin III. Biochemistry 22: 5055–5061, 1983. ; and

[41284] Tsuda, M.; Sei, Y.; Yamamura, M.; Yamamoto, M.; Shino-
hara, Y. : Detection of a new mutant alpha-
1-antichymotrypsin in patients with occlusive-
cerebrovascular disease. FEBS Lett. 304: 66.

[41285] Further studies establishing the function and utilities of
ACT are found in John Hopkins OMIM database record ID
107280, and in cited publications numbered
12428–12442, 78 and 833–839 listed in the bibliography
section hereinbelow, which are also hereby incorporated
by reference. Breast Cancer 1, Early Onset (BRCA1, Acces-
sion NM_007294) is another VGAM1146 host target gene.
BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10 are
HOST TARGET binding sites found in untranslated regions
of mRNA encoded by BRCA1, corresponding to HOST
TARGET binding sites such as BINDING SITE I, BINDING
SITE II or BINDING SITE III. Table 2 illustrates the comple-
mentarity of the nucleotide sequences of BRCA1 BINDING
SITE1 through BRCA1 BINDING SITE10, designated SEQ
ID:14161, SEQ ID:14167, SEQ ID:14173, SEQ ID:14179,
SEQ ID:14186, SEQ ID:14192, SEQ ID:14198, SEQ
ID:14206, SEQ ID:14212 and SEQ ID:14218 respectively,
to the nucleotide sequence of VGAM1146 RNA, herein

designated VGAM RNA, also designated SEQ ID:3857.

[41286] Another function of VGAM1146 is therefore inhibition of Breast Cancer 1, Early Onset (BRCA1, Accession NM_007294). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_032983) is another VGAM1146 host target gene. CASP2 BINDING SITE1 through CASP2 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP2 BINDING SITE1 through CASP2 BINDING SITE4, designated SEQ ID:26857, SEQ ID:26862, SEQ ID:6889 and SEQ ID:6998 respectively, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41287] Another function of VGAM1146 is therefore inhibition of Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-reg-

ulated 2) (CASP2, Accession NM_032983), a gene which involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP2. The function of CASP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM148. Homeo Box A7 (HOXA7, Accession NM_006896) is another VGAM1146 host target gene. HOXA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXA7 BINDING SITE, designated SEQ ID:13770, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41288] Another function of VGAM1146 is therefore inhibition of Homeo Box A7 (HOXA7, Accession NM_006896), a gene which provides cells with specific positional identities on the anterior–posterior axis. Accordingly, utilities of

VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXA7. The function of HOXA7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40) (IL12B, Accession NM_002187) is another VGAM1146 host target gene. IL12B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL12B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL12B BINDING SITE, designated SEQ ID:7942, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41289] Another function of VGAM1146 is therefore inhibition of Interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40) (IL12B, Accession NM_002187). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL12B. Myeloid/

lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529) is another VGAM1146 host target gene. MLLT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT3 BINDING SITE, designated SEQ ID:10871, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41290] Another function of VGAM1146 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529), a gene which is Serine and proline rich protein. Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT3. The function of MLLT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM67.Nephroblastoma Overexpressed Gene (NOV, Ac-

cession NM_002514) is another VGAM1146 host target gene. NOV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NOV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOV BINDING SITE, designated SEQ ID:8346, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41291] Another function of VGAM1146 is therefore inhibition of Nephroblastoma Overexpressed Gene (NOV, Accession NM_002514), a gene which is likely to play a role in cell growth regulation . Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOV. The function of NOV has been established by previous studies. The avian nephroblastoma induced by myeloblastosis-associated virus (MAV) is a good model of Wilms tumor because of histologic similarities. Soret et al. (1989) and Joliot et al. (1992) identified in MAV-1-induced avian nephroblastoma a new protooncogene they called nov for nephroblastoma overexpressed gene. Martinerie and Perbal (1991) found that human sequences homologous to nov were

expressed in normal hematopoietic cells and in 1 nephroblastoma. By a combination of study of somatic cell hybrids and in situ hybridization, Martinerie et al. (1992) showed that the human homolog maps to 8q24.1, proximal to MYC (OMIM Ref. No. 190080). Snaith et al. (1996) stated that the NOV gene encodes a cysteine-rich protein that is overexpressed in avian nephroblastomas. It is a member of the CCN family of proteins that includes connective tissue growth factor (OMIM Ref. No. 121009). These proteins are encoded by a group of genes known as immediate-early genes, so named because they are expressed after induction by growth factors or certain oncogenes. The proteins share several common structural motifs: a consensus sequence present in IGF (insulin-like growth factor)-binding proteins (the IGFBP motif), an oligomeric complex-forming domain first identified in von Willebrand factor (VWF; 193400), a binding domain to soluble and matrix molecules, and a dimerization (CT) domain (Bork, 1993). All CCN family members are thought to be involved in the control of cell proliferation. Snaith et al. (1996) isolated and characterized genomic and cDNA clones encompassing the mouse nov gene. It is highly conserved with the human and chick nov genes at the

level of nucleotide sequence and genomic organization.

The exon structure reflected the modular organization of NOV protein in a number of structural domains. These are highly conserved with other members of the CCN family, as is the distribution of 38 of its 40 cysteine residues.

Snaith et al. (1996) mapped the nov gene to mouse chromosome 15 in a region of conserved synteny with human chromosome 8.

[41292] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41293] Martinerie, C.; Perbal, B. : Expression of a gene encoding a novel potential IGF binding protein in human tissues. C. R. Acad. Sci. (Paris) 313 (ser. 3): 345–351, 1991. ; and

[41294] Snaith, M. R.; Natarajan, D.; Taylor, L. B.; Choi, C.-P.; Martinerie, C.; Perbal, B.; Schofield, P. N.; Boulter, C. A. : Genomic structure and chromosomal mapping of the mouse nov gene.

[41295] Further studies establishing the function and utilities of NOV are found in John Hopkins OMIM database record ID 164958, and in cited publications numbered 10803, 10805–1080 and 11959–10809 listed in the bibliography section hereinbelow, which are also hereby incorporated

by reference. Profilin 2 (PFN2, Accession NM_053024) is another VGAM1146 host target gene. PFN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFN2 BINDING SITE, designated SEQ ID:27582, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41296] Another function of VGAM1146 is therefore inhibition of Profilin 2 (PFN2, Accession NM_053024). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFN2. Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM_020472) is another VGAM1146 host target gene. PIGA BINDING SITE1 through PIGA BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIGA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGA BINDING SITE1

through PIGA BINDING SITE3, designated SEQ ID:21712, SEQ ID:21719 and SEQ ID:8499 respectively, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41297] Another function of VGAM1146 is therefore inhibition of Phosphatidylinositol Glycan, Class A (paroxysmal nocturnal hemoglobinuria) (PIGA, Accession NM_020472). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGA. Chemokine (C-C motif) Receptor 5 (CCR5, Accession NM_000579) is another VGAM1146 host target gene. CCR5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR5 BINDING SITE, designated SEQ ID:6183, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41298] Another function of VGAM1146 is therefore inhibition of Chemokine (C-C motif) Receptor 5 (CCR5, Accession NM_000579). Accordingly, utilities of VGAM1146 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR5. Calsyntenin 2 (CLSTN2, Accession NM_022131) is another VGAM1146 host target gene. CLSTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLSTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN2 BINDING SITE, designated SEQ ID:22693, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41299] Another function of VGAM1146 is therefore inhibition of Calsyntenin 2 (CLSTN2, Accession NM_022131). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLSTN2. CPR2 (Accession NM_030900) is another VGAM1146 host target gene. CPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPR2 BIND-

ING SITE, designated SEQ ID:25176, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41300] Another function of VGAM1146 is therefore inhibition of CPR2 (Accession NM_030900). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPR2. MGC4730 (Accession XM_034644) is another VGAM1146 host target gene. MGC4730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4730 BINDING SITE, designated SEQ ID:32133, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41301] Another function of VGAM1146 is therefore inhibition of MGC4730 (Accession XM_034644). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4730. ODZ2 (Accession XM_047995) is another VGAM1146 host target gene. ODZ2 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by ODZ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ODZ2 BINDING SITE, designated SEQ ID:35097, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41302] Another function of VGAM1146 is therefore inhibition of ODZ2 (Accession XM_047995). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ODZ2. TA-KRP (Accession NM_032505) is another VGAM1146 host target gene. TA-KRP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TA-KRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TA-KRP BINDING SITE, designated SEQ ID:26254, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41303] Another function of VGAM1146 is therefore inhibition of

TA-KRP (Accession NM_032505). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TA-KRP. WD Repeat Domain 7 (WDR7, Accession NM_015285) is another VGAM1146 host target gene. WDR7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WDR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR7 BINDING SITE, designated SEQ ID:17611, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41304] Another function of VGAM1146 is therefore inhibition of WD Repeat Domain 7 (WDR7, Accession NM_015285). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR7. LOC154739 (Accession XM_098602) is another VGAM1146 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41721, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41305] Another function of VGAM1146 is therefore inhibition of LOC154739 (Accession XM_098602). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC158401 (Accession XM_088568) is another VGAM1146 host target gene. LOC158401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158401 BINDING SITE, designated SEQ ID:39837, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41306] Another function of VGAM1146 is therefore inhibition of LOC158401 (Accession XM_088568). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158401. LOC90488 (Accession XM_032129) is another VGAM1146 host target gene. LOC90488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90488 BINDING SITE, designated SEQ ID:31559, to the nucleotide sequence of VGAM1146 RNA, herein designated VGAM RNA, also designated SEQ ID:3857.

[41307] Another function of VGAM1146 is therefore inhibition of LOC90488 (Accession XM_032129). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90488. LOC91115 (Accession XM_036218) is another VGAM1146 host target gene. LOC91115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91115 BINDING SITE, designated SEQ ID:32403, to the nucleotide sequence of VGAM1146 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3857.

[41308] Another function of VGAM1146 is therefore inhibition of LOC91115 (Accession XM_036218). Accordingly, utilities of VGAM1146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91115. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1147 (VGAM1147) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41309] VGAM1147 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1147 was detected is described hereinabove with reference to Figs. 1–8.

[41310] VGAM1147 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41311] VGAM1147 gene encodes a VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1147 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1147 precursor RNA is designated SEQ ID:1133, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1133 is located at position 216748 relative to the genome of Fowlpox Virus.

- [41312] VGAM1147 precursor RNA folds onto itself, forming VGAM1147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41313] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1147 folded precursor RNA into VGAM1147 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1147 RNA is designated SEQ ID:3858, and is provided hereinbelow with reference to the sequence listing part.

[41314] VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1147 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41315] VGAM1147 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1147 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1147 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[41316] The complementary binding of VGAM1147 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1147 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1147 host target RNA into VGAM1147 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41317] It is appreciated that VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1147 host target genes. The mRNA of

each one of this plurality of VGAM1147 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1147 RNA, herein designated VGAM RNA, and which when bound by VGAM1147 RNA causes inhibition of translation of respective one or more VGAM1147 host target proteins.

[41318] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1147 gene, herein designated VGAM GENE, on one or more VGAM1147 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[41319] It is yet further appreciated that a function of VGAM1147 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1147 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1147 correlate with, and may be deduced from, the identity of the host target genes which VGAM1147 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41320] Nucleotide sequences of the VGAM1147 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1147 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1147 are further described hereinbelow with reference to Table 1.

[41321] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1147 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1147 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41322] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1147 gene, herein designated VGAM is inhibition of expression of VGAM1147 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1147 correlate with, and may be deduced from, the identity of the target genes which VGAM1147 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41323] Holocarboxylase Synthetase

(biotin-[propionyl-Coenzyme A-carboxylase (ATP-hydrolysing)] Ligase) (HLCS, Accession NM_000411) is a VGAM1147 host target gene. HLCS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLCS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLCS BINDING SITE, designated SEQ ID:5988, to the nucleotide sequence of VGAM1147 RNA, herein designated VGAM RNA, also designated SEQ ID:3858.

[41324] A function of VGAM1147 is therefore inhibition of Holo-

carboxylase Synthetase (biotin-[propionyl-Coenzyme A-carboxylase (ATP-hydrolysing)] Ligase) (HLCS, Accession NM_000411). Accordingly, utilities of VGAM1147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLCS. Tumor Necrosis Factor (ligand) Superfamily, Member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa) (TNFSF4, Accession NM_003326) is another VGAM1147 host target gene. TNFSF4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF4 BINDING SITE, designated SEQ ID:9327, to the nucleotide sequence of VGAM1147 RNA, herein designated VGAM RNA, also designated SEQ ID:3858.

[41325] Another function of VGAM1147 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa) (TNFSF4, Accession NM_003326), a gene which co-stimulates t cell proliferation and cytokine production. Accordingly, utilities of VGAM1147 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with TNFSF4. The function of TNFSF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM463.FLJ23511 (Accession NM_032239) is another VGAM1147 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25969, to the nucleotide sequence of VGAM1147 RNA, herein designated VGAM RNA, also designated SEQ ID:3858.

[41326] Another function of VGAM1147 is therefore inhibition of FLJ23511 (Accession NM_032239). Accordingly, utilities of VGAM1147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. LOC120196 (Accession XM_061916) is another VGAM1147 host target gene. LOC120196 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC120196, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120196 BINDING SITE, designated SEQ ID:37218, to the nucleotide sequence of VGAM1147 RNA, herein designated VGAM RNA, also designated SEQ ID:3858.

[41327] Another function of VGAM1147 is therefore inhibition of LOC120196 (Accession XM_061916). Accordingly, utilities of VGAM1147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120196. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1148 (VGAM1148) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41328] VGAM1148 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1148 was detected is described hereinabove with reference to Figs. 1-8.

[41329] VGAM1148 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Her-

pesvirus 7. VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41330] VGAM1148 gene encodes a VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1148 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1148 precursor RNA is designated SEQ ID:1134, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1134 is located at position 73086 relative to the genome of Cercopithecine Herpesvirus 7.

[41331] VGAM1148 precursor RNA folds onto itself, forming VGAM1148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41332] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1148 folded precursor RNA into VGAM1148 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1148 RNA is designated SEQ ID:3859, and is provided hereinbelow with reference to the sequence listing part.

[41333] VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1148 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41334] VGAM1148 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1148 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1148 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41335] The complementary binding of VGAM1148 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1148 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1148 host target RNA into VGAM1148 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41336] It is appreciated that VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1148 host target genes. The mRNA of each one of this plurality of VGAM1148 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1148 RNA, herein designated VGAM RNA, and which when bound by VGAM1148 RNA causes inhibition of translation of respective one or more VGAM1148 host target proteins.

[41337] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1148 gene, herein designated VGAM GENE, on one or more VGAM1148 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41338] It is yet further appreciated that a function of VGAM1148 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1148 correlate with, and may be deduced from, the identity of the host target genes which VGAM1148 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41339] Nucleotide sequences of the VGAM1148 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1148 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1148 are further described hereinbelow with reference to Table 1.

[41340] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1148 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1148 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41341] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1148 gene, herein designated VGAM is inhibition of expression of VGAM1148 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1148 correlate with, and may be deduced from, the identity of the target genes which VGAM1148 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41342] Disabled Homolog 2, Mitogen-responsive Phosphoprotein (Drosophila) (DAB2, Accession NM_001343) is a VGAM1148 host target gene. DAB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAB2 BINDING SITE,

designated SEQ ID:7023, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41343] A function of VGAM1148 is therefore inhibition of Disabled Homolog 2, Mitogen-responsive Phosphoprotein (Drosophila) (DAB2, Accession NM_001343), a gene which may be a component of the csf-1 signal transduction pathway. Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAB2. The function of DAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM659.FLJ11269 (Accession XM_052193) is another VGAM1148 host target gene. FLJ11269 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11269, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11269 BINDING SITE, designated SEQ ID:35955, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41344] Another function of VGAM1148 is therefore inhibition of FLJ11269 (Accession XM_052193). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11269. KIAA0016 (Accession NM_014765) is another VGAM1148 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16536, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41345] Another function of VGAM1148 is therefore inhibition of KIAA0016 (Accession NM_014765). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. KIAA1431 (Accession XM_032055) is another VGAM1148 host target gene. KIAA1431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1431, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1431 BINDING SITE, designated SEQ ID:31551, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41346] Another function of VGAM1148 is therefore inhibition of KIAA1431 (Accession XM_032055). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1431. Protocadherin 19 (PCDH19, Accession XM_033173) is another VGAM1148 host target gene. PCDH19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH19 BINDING SITE, designated SEQ ID:31866, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41347] Another function of VGAM1148 is therefore inhibition of Protocadherin 19 (PCDH19, Accession XM_033173). Accordingly, utilities of VGAM1148 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with PCDH19. LOC221300 (Accession XM_166322) is another VGAM1148 host target gene. LOC221300 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221300 BINDING SITE, designated SEQ ID:44150, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41348] Another function of VGAM1148 is therefore inhibition of LOC221300 (Accession XM_166322). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221300. LOC222499 (Accession XM_169457) is another VGAM1148 host target gene. LOC222499 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC222499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC222499 BINDING SITE, designated SEQ ID:45303, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41349] Another function of VGAM1148 is therefore inhibition of LOC222499 (Accession XM_169457). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222499. LOC90321 (Accession XM_030896) is another VGAM1148 host target gene. LOC90321 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90321, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90321 BINDING SITE, designated SEQ ID:31210, to the nucleotide sequence of VGAM1148 RNA, herein designated VGAM RNA, also designated SEQ ID:3859.

[41350] Another function of VGAM1148 is therefore inhibition of LOC90321 (Accession XM_030896). Accordingly, utilities of VGAM1148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90321. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1149 (VGAM1149) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41351] VGAM1149 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1149 was detected is described hereinabove with reference to Figs. 1–8.

[41352] VGAM1149 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41353] VGAM1149 gene encodes a VGAM1149 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1149 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1149 precursor RNA is designated SEQ ID:1135, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1135 is located at position 75465 relative to the

genome of Cercopithecine Herpesvirus 7.

[41354] VGAM1149 precursor RNA folds onto itself, forming VGAM1149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41355] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1149 folded precursor RNA into VGAM1149 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1149 RNA is designated SEQ ID:3860, and is provided hereinbelow with reference to the sequence listing part.

[41356] VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1149 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41357] VGAM1149 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1149 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1149 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[41358] The complementary binding of VGAM1149 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1149 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1149 host target RNA into VGAM1149 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41359] It is appreciated that VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1149 host target genes. The mRNA of each one of this plurality of VGAM1149 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1149 RNA, herein designated VGAM RNA, and which when bound by VGAM1149 RNA causes inhibition of translation of respective one or more VGAM1149 host target proteins.

[41360] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1149 gene, herein designated VGAM GENE, on one or more VGAM1149 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41361] It is yet further appreciated that a function of VGAM1149 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of

VGAM1149 correlate with, and may be deduced from, the identity of the host target genes which VGAM1149 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41362] Nucleotide sequences of the VGAM1149 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1149 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1149 are further described hereinbelow with reference to Table 1.

[41363] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1149 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1149 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41364] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1149 gene, herein designated VGAM is inhibition of expression of VGAM1149 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1149 correlate with, and may be deduced

from, the identity of the target genes which VGAM1149 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41365] Lipoprotein Lipase (LPL, Accession NM_000237) is a VGAM1149 host target gene. LPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPL BINDING SITE, designated SEQ ID:5747, to the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, also designated SEQ ID:3860.

[41366] A function of VGAM1149 is therefore inhibition of Lipoprotein Lipase (LPL, Accession NM_000237), a gene which is the hydrolysis of triglycerides of circulating chylomicrons and very low density lipoproteins (vldl). the enzyme functions in the presence of apolipoprotein c-2 on the luminal surface of vascular. Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPL. The function of LPL and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM55.Dicer1, Dcr-1 Homolog (Drosophila) (DICER1, Accession NM_030621) is another VGAM1149 host target gene. DICER1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DICER1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DICER1 BINDING SITE, designated SEQ ID:24963, to the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, also designated SEQ ID:3860.

[41367] Another function of VGAM1149 is therefore inhibition of Dicer1, Dcr-1 Homolog (Drosophila) (DICER1, Accession NM_030621). Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DICER1. FLJ11040 (Accession NM_018307) is another VGAM1149 host target gene. FLJ11040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ11040 BINDING SITE, designated SEQ ID:20294, to the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, also designated SEQ ID:3860.

[41368] Another function of VGAM1149 is therefore inhibition of FLJ11040 (Accession NM_018307). Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11040. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_020552) is another VGAM1149 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING SITE4, designated SEQ ID:21770, SEQ ID:21761, SEQ ID:14843 and SEQ ID:15767 respectively, to the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, also designated SEQ ID:3860.

[41369] Another function of VGAM1149 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession

NM_020552). Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. LOC253747 (Accession XM_173619) is another VGAM1149 host target gene. LOC253747 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253747 BINDING SITE, designated SEQ ID:46551, to the nucleotide sequence of VGAM1149 RNA, herein designated VGAM RNA, also designated SEQ ID:3860.

[41370] Another function of VGAM1149 is therefore inhibition of LOC253747 (Accession XM_173619). Accordingly, utilities of VGAM1149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253747. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1150 (VGAM1150) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[41371] VGAM1150 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1150 was detected is described hereinabove with reference to Figs. 1–8.

[41372] VGAM1150 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41373] VGAM1150 gene encodes a VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1150 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1150 precursor RNA is designated SEQ ID:1136, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1136 is located at position 76231 relative to the genome of Cercopithecine Herpesvirus 7.

[41374] VGAM1150 precursor RNA folds onto itself, forming VGAM1150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41375] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1150 folded precursor RNA into VGAM1150 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1150 RNA is designated SEQ ID:3861, and is provided hereinbelow with reference to the sequence listing part.

[41376] VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1150 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[41377] VGAM1150 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1150 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1150 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[41378] The complementary binding of VGAM1150 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1150 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1150 host target RNA into VGAM1150 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41379] It is appreciated that VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1150 host target genes. The mRNA of each one of this plurality of VGAM1150 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1150 RNA, herein designated VGAM RNA, and which when bound by VGAM1150 RNA causes inhibition of translation of respective one or more VGAM1150 host target proteins.

[41380] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1150 gene, herein designated VGAM GENE, on one

or more VGAM1150 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41381] It is yet further appreciated that a function of VGAM1150 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1150 correlate with, and may be deduced from, the identity of the host target genes which VGAM1150 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41382] Nucleotide sequences of the VGAM1150 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1150 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1150 are further described hereinbelow with reference to Table 1.

[41383] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1150 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1150 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41384] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1150 gene, herein designated VGAM is inhibition of expression of VGAM1150 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1150 correlate with, and may be deduced from, the identity of the target genes which VGAM1150 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41385] Integrin, Beta 1 (fibronectin receptor, beta polypeptide,

antigen CD29 includes MDF2, MSK12) (ITGB1, Accession NM_002211) is a VGAM1150 host target gene. ITGB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB1 BINDING SITE, designated SEQ ID:7977, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also designated SEQ ID:3861.

[41386] A function of VGAM1150 is therefore inhibition of Integrin, Beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12) (ITGB1, Accession NM_002211), a gene which acts as a fibronectin receptor. Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB1. The function of ITGB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM427. Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM_011181) is another VGAM1150 host target gene. LRAT BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by LRAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRAT BINDING SITE, designated SEQ ID:30182, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also designated SEQ ID:3861.

[41387] Another function of VGAM1150 is therefore inhibition of Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM_011181). Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRAT. FLJ20281 (Accession XM_165663) is another VGAM1150 host target gene. FLJ20281 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20281 BINDING SITE, designated SEQ ID:43728, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3861.

[41388] Another function of VGAM1150 is therefore inhibition of FLJ20281 (Accession XM_165663). Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20281. RP4-622L5 (Accession NM_019118) is another VGAM1150 host target gene. RP4-622L5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP4-622L5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP4-622L5 BINDING SITE, designated SEQ ID:21200, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also designated SEQ ID:3861.

[41389] Another function of VGAM1150 is therefore inhibition of RP4-622L5 (Accession NM_019118). Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP4-622L5. LOC129566 (Accession XM_065294) is another VGAM1150 host target gene. LOC129566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129566, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129566 BINDING SITE, designated SEQ ID:37280, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also designated SEQ ID:3861.

[41390] Another function of VGAM1150 is therefore inhibition of LOC129566 (Accession XM_065294). Accordingly, utilities of VGAM1150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129566. LOC154386 (Accession XM_087920) is another VGAM1150 host target gene. LOC154386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154386 BINDING SITE, designated SEQ ID:39472, to the nucleotide sequence of VGAM1150 RNA, herein designated VGAM RNA, also designated SEQ ID:3861.

[41391] Another function of VGAM1150 is therefore inhibition of LOC154386 (Accession XM_087920). Accordingly, utilities of VGAM1150 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC154386. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1151 (VGAM1151) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41392] VGAM1151 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1151 was detected is described hereinabove with reference to Figs. 1–8.

[41393] VGAM1151 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41394] VGAM1151 gene encodes a VGAM1151 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1151 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1151 precursor RNA is desig-

nated SEQ ID:1137, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1137 is located at position 2018 relative to the genome of Cowpox Virus.

- [41395] VGAM1151 precursor RNA folds onto itself, forming VGAM1151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41396] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1151 folded precursor RNA into VGAM1151 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1151 RNA is designated SEQ ID:3862, and is provided hereinbelow with reference to the sequence

listing part.

[41397] VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1151 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41398] VGAM1151 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1151 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1151 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41399] The complementary binding of VGAM1151 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1151 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1151 host target RNA into VGAM1151 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41400] It is appreciated that VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1151 host target genes. The mRNA of each one of this plurality of VGAM1151 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1151 RNA, herein designated VGAM

RNA, and which when bound by VGAM1151 RNA causes inhibition of translation of respective one or more VGAM1151 host target proteins.

[41401] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1151 gene, herein designated VGAM GENE, on one or more VGAM1151 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41402] It is yet further appreciated that a function of VGAM1151 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1151 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1151 correlate with, and may be deduced from, the identity of the host target genes which VGAM1151 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41403] Nucleotide sequences of the VGAM1151 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1151 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1151 are further described hereinbelow with reference to Table 1.

[41404] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1151 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1151 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41405] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1151 gene, herein designated VGAM is

inhibition of expression of VGAM1151 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1151 correlate with, and may be deduced from, the identity of the target genes which VGAM1151 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41406] 1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession NM_006412) is a VGAM1151 host target gene. AGPAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AGPAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGPAT2 BINDING SITE, designated SEQ ID:13120, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41407] A function of VGAM1151 is therefore inhibition of 1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta) (AGPAT2, Accession NM_006412). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with AGPAT2. Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM_042963) is another VGAM1151 host target gene. ARHGEF6 BINDING SITE1 and ARHGEF6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ARHGEF6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF6 BINDING SITE1 and ARHGEF6 BINDING SITE2, designated SEQ ID:33846 and SEQ ID:33847 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41408] Another function of VGAM1151 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM_042963). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. Bassoon (presynaptic cytomatrix protein) (BSN, Accession NM_003458) is another VGAM1151 host target gene. BSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BSN, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BSN BINDING SITE, designated SEQ ID:9517, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41409] Another function of VGAM1151 is therefore inhibition of Bassoon (presynaptic cytomatrix protein) (BSN, Accession NM_003458), a gene which may be involved in cytomatrix organization at the site of neurotransmitter release. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BSN. The function of BSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM638. Dihydropyrimidinase-like 2 (DPYSL2, Accession NM_001386) is another VGAM1151 host target gene. DPYSL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DPYSL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL2 BINDING SITE, designated SEQ

ID:7063, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41410] Another function of VGAM1151 is therefore inhibition of Dihydropyrimidinase-like 2 (DPYSL2, Accession NM_001386), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL2. The function of DPYSL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Enolase 2, (gamma, neuronal) (ENO2, Accession NM_001975) is another VGAM1151 host target gene. ENO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENO2 BINDING SITE, designated SEQ ID:7706, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41411] Another function of VGAM1151 is therefore inhibition of

Enolase 2, (gamma, neuronal) (ENO2, Accession NM_001975), a gene which converts 2-phospho-D-glycerate to phosphoenolpyruvate in glycolysis. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENO2. The function of ENO2 has been established by previous studies. The enolases (phosphopyruvate hydratase; EC 4.2.1.11) catalyze the interconversion of 2-phosphoglycerate to phosphoenolpyruvate in the glycolytic pathway. The functional enzyme is a dimer made up of subunits referred to as alpha, beta, and gamma. In mammals there are at least 3 isoforms of enolase characterized by different tissue distributions as well as by distinct biochemical and immunologic properties. The alpha-, or nonneuronal, enolase (ENO1; 172430) is a nearly ubiquitous form, found in almost all tissues, and its expression precedes that of the other isoforms in the early stage of embryonic development. The beta-, or muscle-specific, enolase (ENO3; 131370) is present in adult skeletal muscle, and the gamma-, or neuron-specific, enolase (ENO2) is the major form found in mature neurons and in cells of neuronal origin. Enolase-2 is determined by a gene on chromo-

some 12 (Grzeschik, 1976). Herbschleb-Voogt et al. (1978) confirmed assignment to chromosome 12 by showing synteny with LDHB and PEPB in man-mouse hybrids. Mattei et al. (1982) assigned ENO2 to 12p11-qter by study of cells trisomic for 12pter-p11. Law and Kao (1982) also assigned the gene to chromosome 12. By in situ hybridization, Craig et al. (1989, 1990) localized ENO2 to 12p13. Oliva et al. (1991) demonstrated that the ENO2 gene contains 12 exons distributed over 9,213 nucleotides. The putative promoter region lacks canonical TATA and CAAT boxes, is very G+C-rich, and contains several potential regulatory sequences.

[41412] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41413] Oliva, D.; Cali, L.; Feo, S.; Giallongo, A. : Complete structure of the human gene encoding neuron-specific enolase. *Genomics* 10: 157-165, 1991. ; and

[41414] Hinks, L. J.; Day, I. N. M. : Further studies of enolase loci. (Abstract) *Cytogenet. Cell Genet.* 58: 1854 only, 1991.

[41415] Further studies establishing the function and utilities of ENO2 are found in John Hopkins OMIM database record ID 131360, and in cited publications numbered 4575-4583

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FtsJ Homolog 2 (E. coli) (FTSJ2, Accession NM_013393) is another VGAM1151 host target gene. FTSJ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FTSJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FTSJ2 BINDING SITE, designated SEQ ID:15044, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41416] Another function of VGAM1151 is therefore inhibition of FtsJ Homolog 2 (E. coli) (FTSJ2, Accession NM_013393). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FTSJ2. GAC1 (Accession NM_006338) is another VGAM1151 host target gene. GAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

GAC1 BINDING SITE, designated SEQ ID:13037, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41417] Another function of VGAM1151 is therefore inhibition of GAC1 (Accession NM_006338). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAC1. Glutamate Dehydrogenase 1 (GLUD1, Accession NM_005271) is another VGAM1151 host target gene. GLUD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLUD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLUD1 BINDING SITE, designated SEQ ID:11774, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41418] Another function of VGAM1151 is therefore inhibition of Glutamate Dehydrogenase 1 (GLUD1, Accession NM_005271). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLUD1. Hyperpolarization

Activated Cyclic Nucleotide-gated Potassium Channel 4 (HCN4, Accession NM_005477) is another VGAM1151 host target gene. HCN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCN4 BINDING SITE, designated SEQ ID:11979, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41419] Another function of VGAM1151 is therefore inhibition of Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 4 (HCN4, Accession NM_005477), a gene which is hyperpolarization activated cyclic nucleotide-gated cation channel 4 and may act as a pacemaker channel in the heart . Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCN4. The function of HCN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.High Mobility Group AT-hook 2 (HMGA2, Ac-

cession NM_003483) is another VGAM1151 host target gene. HMGA2 BINDING SITE1 and HMGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HMGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE1 and HMGA2 BINDING SITE2, designated SEQ ID:9566 and SEQ ID:9567 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41420] Another function of VGAM1151 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Kinesin Family Member 3B (KIF3B, Accession NM_004798) is another VGAM1151 host

target gene. KIF3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3B BINDING SITE, designated SEQ ID:11216, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41421] Another function of VGAM1151 is therefore inhibition of Kinesin Family Member 3B (KIF3B, Accession NM_004798), a gene which is a microtubule-based anterograde translocator for membranous organelles. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF3B. The function of KIF3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1017. Lipoprotein Lipase (LPL, Accession NM_000237) is another VGAM1151 host target gene. LPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPL, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPL BINDING SITE, designated SEQ ID:5754, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41422] Another function of VGAM1151 is therefore inhibition of Lipoprotein Lipase (LPL, Accession NM_000237), a gene which is the hydrolysis of triglycerides of circulating chylomicrons and very low density lipoproteins (vldl). the enzyme functions in the presence of apolipoprotein c-2 on the luminal surface of vascular. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPL. The function of LPL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog (mouse) (MEIS1, Accession NM_002398) is another VGAM1151 host target gene. MEIS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEIS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of MEIS1 BINDING SITE, designated SEQ ID:8218, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41423] Another function of VGAM1151 is therefore inhibition of Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog (mouse) (MEIS1, Accession NM_002398), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEIS1. The function of MEIS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894. Nuclear Factor I/A (NFIA, Accession XM_046827) is another VGAM1151 host target gene. NFIA BINDING SITE1 and NFIA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NFIA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFIA BINDING SITE1 and NFIA BINDING SITE2, designated SEQ ID:34841 and SEQ ID:34840 respectively, to the nu-

cleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41424] Another function of VGAM1151 is therefore inhibition of Nuclear Factor I/A (NFIA, Accession XM_046827). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFIA. Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180) is another VGAM1151 host target gene. NTRK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTRK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTRK2 BINDING SITE, designated SEQ ID:12843, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41425] Another function of VGAM1151 is therefore inhibition of Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180), a gene which is involved in the development and/or maintenance of the nervous system. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with NTRK2. The function of NTRK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341. Paired Box Gene 5 (B-cell lineage specific activator protein) (PAX5, Accession NM_016734) is another VGAM1151 host target gene. PAX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAX5 BINDING SITE, designated SEQ ID:18792, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41426] Another function of VGAM1151 is therefore inhibition of Paired Box Gene 5 (B-cell lineage specific activator protein) (PAX5, Accession NM_016734), a gene which plays a role in B-cell differentiation, neural development and spermatogenesis. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX5. The function of PAX5 has been established by previous studies. The PAX5

gene is located in the 9p13 region, which is involved in t(9;14)(p13;q32) translocations recurring in small lymphocytic lymphomas of the plasmacytoid subtype and in derived large cell lymphomas. Ohno et al. (1990) showed that in a diffuse large cell lymphoma (KIS-1) with a translocation, the immunoglobulin heavy-chain (IgH) locus on 14q32 is juxtaposed to 9p13 sequences of unknown function. Busslinger et al. (1996) showed that the KIS-1 translocation breakpoint is located 1,807 bp upstream of exon 1A of PAX5, thus bringing the potent E-mu enhancer of the IgH gene into close proximity with the PAX5 promoters. The data suggested to them that deregulation of PAX5 gene transcription by the t(9;14) translocation contributes to the pathogenesis of small lymphocytic lymphomas with plasmacytoid differentiation. In addition to immunoglobulin V genes, the 5-prime sequences of BCL6 (OMIM Ref. No. 109565) and FAS (TNFRSF6; 134637) are mutated in normal germinal center B lymphocytes. Genomic instability promotes tumorigenesis through defective chromosome segregation and DNA mismatch repair inactivation. By screening 18 loci for mutations, Pasqualucci et al. (2001) identified changes in the germline sequences of PIM1 (OMIM Ref. No. 164960), MYC

(OMIM Ref. No. 190080), ARHH (OMIM Ref. No. 602037), and/or PAX5, in addition to BCL6, in a majority of diffuse large cell lymphomas (DLCLs; OMIM Ref. No. 601889). No mutations in PIM1, MYC, ARHH, and PAX5 were detected in germinal-center lymphocytes, naive B cells, or B-cell malignancies other than DLCLs. PAX5 mutations, which were observed in 57% of DLCLs, were identified downstream of both transcription sites, predominantly in non-coding sequences around exon 1B. FISH analysis indicated that hypermutation in these genes is not due to chromosomal translocation, as seen in Burkitt lymphoma (OMIM Ref. No. 113970). Chromosomal translocation, however, may be an outcome of hypermutation. Specific features of the hypermutation process, including the predominance of single nucleotide substitutions with occasional deletions or duplications, a preference for transitions over transversions, and a specific motif targeting RGYW, were recognizable in each of the hypermutated loci.

Pasqualucci et al. (2001) proposed that aberrant hypermutation of regulatory and coding sequences of genes that do not represent physiologic targets may provide the basis for DLCL pathogenesis and explain its phenotypic and clinical heterogeneity. This hypermutation malfunc-

tion is unlikely to be due to defective DNA mismatch repair and does not appear to involve activation-induced deaminase (AICDA; 605257). Animal model experiments lend further support to the function of PAX5. Nutt et al. (1999) demonstrated that pro-B cells lacking Pax5 are incapable of in vitro B-cell differentiation unless Pax5 expression is restored by retroviral transduction. Pax5 $-/-$ pro-B cells are not restricted in their lineage fate, as stimulation with appropriate cytokines induces them to differentiate into functional macrophages, osteoclasts, dendritic cells, granulocytes, and natural killer cells. As expected for a clonogenic hematopoietic progenitor with lymphomyeloid developmental potential, the Pax5 $-/-$ pro-B cell expresses genes of different lineage-affiliated programs, and restoration of Pax5 activity represses this lineage-promiscuous transcription. Pax5 therefore plays an essential role in B-lineage commitment by suppressing alternative lineage choices. Differentiation of the hematopoietic stem cell into distinct blood cell types was thought to progress through intermediate progenitor cells with restricted developmental potential. This view of hematopoiesis was challenged by the findings of Nutt et al. (1999) that the Pax5 $-/-$ pro-B cell possesses, at least

under in vitro conditions, a broad, developmental potential similar to that of the hematopoietic stem cell itself. However, Pax5 $-/-$ pro-B cells are unable to differentiate along the erythroid and megakaryocytic lineages, and cannot reconstitute the entire hematopoietic system under transplantation experiments. Therefore, Nutt et al. (1999) concluded that the Pax5 $-/-$ pro-B cell must be classified as a hematopoietic progenitor cell with broad lymphoid and myeloid differentiation potential. Nutt et al. (1999) also concluded that their data supported the notion that B-lineage commitment is a stochastic rather than a deterministic process.

[41427] It is appreciated that the abovementioned animal model for PAX5 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[41428] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41429] Pasqualucci, L.; Neumeister, P.; Goossens, T.; Nanjangud, G.; Chaganti, R. S. K.; Kuppers, R.; Dalla-Favera, R. : Hypermutation of multiple proto-oncogenes in B-cell diffuse large-cell lymphomas. Nature 412: 341–346, 2001. ; and

[41430] Nutt, S. L.; Heavey, B.; Rolink, A. G.; Busslinger, M. : Commitment to the B-lymphoid lineage depends on the transcription factor Pax5. Nature 401: 556–562, 1999.

[41431] Further studies establishing the function and utilities of PAX5 are found in John Hopkins OMIM database record ID 167414, and in cited publications numbered 10765–10770, 11110, 1077 and 10772–10773 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Alpha 1 (PCDHA1, Accession NM_018900) is another VGAM1151 host target gene. PCDHA1 BINDING SITE1 through PCDHA1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 through PCDHA1 BINDING SITE4, designated SEQ ID:20866, SEQ ID:20869, SEQ ID:25385 and SEQ ID:25388 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41432] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_018900).

Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_031860) is another VGAM1151 host target gene. PCDHA10 BINDING SITE1 through PCDHA10 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 through PCDHA10 BINDING SITE4, designated SEQ ID:25620, SEQ ID:20876, SEQ ID:20879 and SEQ ID:20886 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41433] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_031860). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 12 (PCDHA12, Accession NM_018903) is another VGAM1151 host target gene. PCDHA12 BINDING SITE1 and PCDHA12 BINDING SITE2 are HOST TARGET binding

sites found in untranslated regions of mRNA encoded by PCDHA12, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA12 BINDING SITE1 and PCDHA12 BINDING SITE2, designated SEQ ID:20897 and SEQ ID:20900 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41434] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 12 (PCDHA12, Accession NM_018903). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA12. Protocadherin Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM1151 host target gene. PCDHA13 BINDING SITE1 and PCDHA13 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE1 and PCDHA13 BINDING SITE2, designated SEQ ID:20910 and SEQ

ID:20917 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41435] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM1151 host target gene. PCDHA3 BINDING SITE1 and PCDHA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE1 and PCDHA3 BINDING SITE2, designated SEQ ID:20927 and SEQ ID:20930 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41436] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM1151 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM1151 host target gene. PCDHA4 BINDING SITE1 and PCDHA4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE1 and PCDHA4 BINDING SITE2, designated SEQ ID:20940 and SEQ ID:20947 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41437] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 6 (PCDHA6, Accession NM_018909) is another VGAM1151 host target gene. PCDHA6 BINDING SITE1 through PCDHA6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 through PCDHA6 BINDING SITE4, designated SEQ ID:20957, SEQ ID:20960, SEQ ID:25589 and SEQ ID:25592 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41438] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 6 (PCDHA6, Accession NM_018909). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 7 (PCDHA7, Accession NM_018910) is another VGAM1151 host target gene. PCDHA7 BINDING SITE1 and PCDHA7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA7 BINDING SITE1 and PCDHA7 BINDING SITE2, designated SEQ ID:20970 and SEQ ID:20977 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41439] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 7 (PCDHA7, Accession NM_018910). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA7. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM1151 host target gene. PCDHA9 BINDING SITE1 and PCDHA9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE1 and PCDHA9 BINDING SITE2, designated SEQ ID:25603 and SEQ ID:25606 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41440] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM1151 host target gene. PCDHAC1 BINDING SITE1 and PCDHAC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHAC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE1 and PCDHAC1 BINDING SITE2, designated SEQ ID:20849 and SEQ ID:20856 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41441] Another function of VGAM1151 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. PCTAIRE Protein Kinase 1 (PCTK1, Accession NM_006201) is another VGAM1151 host target gene. PCTK1 BINDING SITE1 through PCTK1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

PCTK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTK1 BINDING SITE1 through PCTK1 BINDING SITE3, designated SEQ ID:12872, SEQ ID:26907 and SEQ ID:26913 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41442] Another function of VGAM1151 is therefore inhibition of PCTAIRE Protein Kinase 1 (PCTK1, Accession NM_006201), a gene which may play a role in signal transduction cascades in terminally differentiated cells. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCTK1. The function of PCTK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM75. Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM_138934) is another VGAM1151 host target gene. PPT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT2 BINDING SITE, designated SEQ ID:29061, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41443] Another function of VGAM1151 is therefore inhibition of Palmitoyl-protein Thioesterase 2 (PPT2, Accession NM_138934), a gene which is a palmitoyl-protein thioesterase 2 which possesses a different substrate specificity than PPT1. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT2. The function of PPT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Protein Tyrosine Kinase 2 Beta (PTK2B, Accession NM_004103) is another VGAM1151 host target gene. PTK2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTK2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK2B BINDING SITE, designated SEQ

ID:10313, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41444] Another function of VGAM1151 is therefore inhibition of Protein Tyrosine Kinase 2 Beta (PTK2B, Accession NM_004103), a gene which is involved in calcium induced regulation of ion channel and activation of the map kinase signaling pathway. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK2B. The function of PTK2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM555. Runt-related Transcription Factor 3 (RUNX3, Accession NM_004350) is another VGAM1151 host target gene. RUNX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX3 BINDING SITE, designated SEQ ID:10550, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ

ID:3862.

[41445] Another function of VGAM1151 is therefore inhibition of Runt-related Transcription Factor 3 (RUNX3, Accession NM_004350), a gene which binds to the core site, 5'-pygpyggt-3', of a number of enhancers and promoters. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX3. The function of RUNX3 has been established by previous studies. Levanon et al. (1994) isolated and characterized cDNAs corresponding to 3 human 'runt domain'-containing genes: AML1 (RUNX1; 151385), CBFA3, and CBFA1 (RUNX2; 600211). In addition to homology in the highly conserved runt domain, extensive sequence similarities were also observed in other parts of the deduced proteins. All 3 genes carried an identical putative ATP-binding site, -GRSGRGKS-, and their C-terminal halves were particularly rich in proline and serine residues. AML1 cDNAs had been cloned by others, whereas CBFA3 represented a new member of the runt domain gene family, and CBFA1 was identified as the human homolog of the mouse PEBP2A gene. Bae et al. (1995) also cloned and characterized RUNX3, which they termed PEBP2-alpha-C. By genomic sequence analysis,

Bae et al. (1995) determined that the RUNX3 gene contains at least 5 exons. By fluorescence in situ hybridization, Levanon et al. (1994) mapped the CBFA3 gene to 1p36. By FISH, Bae et al. (1995) mapped the RUNX3 gene to 1p36.13–p36.11. Avraham et al. (1995) mapped the homologous gene to mouse chromosome 4. By Southern blot analysis of hybrid cell lines containing different parts of human chromosome 1 and by fluorescence in situ hybridization, Wijmenga et al. (1995) assigned the CBFA3 gene to 1p35–pter. Li et al. (2002) showed that between 45 and 60% of human gastric cancer (OMIM Ref. No. 137215) cells do not significantly express RUNX3 due to hemizygous deletion and hypermethylation of the RUNX3 promoter region. Tumorigenicity of human gastric cancer cell lines in nude mice was inversely related to their level of RUNX3 expression. The authors identified a heterozygous C-to-T transition in the RUNX3 gene, resulting in an arg122-to-cys (R122C) change within the conserved Runt domain of the protein, in 1 gastric carcinoma tissue of 119 examined. Arginine at position 122 is conserved in both nematodes and humans. A tumorigenesis assay in nude mice showed that the R122C change abolished the tumor-suppressive effect of RUNX3, suggesting that a

lack of RUNX3 function is causally related to the genesis and progression of human gastric cancer. However, matching normal tissue was not available in this case and therefore it was not possible to establish whether the observed R122C change was a single-nucleotide polymorphism or a true mutation. Animal model experiments lend further support to the function of RUNX3. Li et al. (2002) generated mice with a targeted disruption of the Runx3 gene. The gastric mucosa of these mice exhibited hyperplasias due to stimulated proliferation and suppressed apoptosis in epithelial cells, and the cells were resistant to growth-inhibitory and apoptosis-inducing actions of transforming growth factor-beta (OMIM Ref. No. 190180), indicating that Runx3 is a major growth regulator of gastric epithelial cells. Inoue et al. (2002) generated Runx3-deficient mice and showed that proprioceptive afferent axons failed to project to their targets in the spinal cord as well as those in the muscle. In contrast, the afferent projections that convey nociception, thermoreception, and mechanoreception signals appeared normal. The mutant mice displayed severe limb ataxia and motor discoordination similar to that of Etv1 (OMIM Ref. No. 600541) mutant mice. Inoue et al. (2002) concluded that Runx3 is

critical in regulating a subpopulation of dorsal root ganglion neurons.

[41446] It is appreciated that the abovementioned animal model for RUNX3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[41447] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41448] Li, Q.-L.; Ito, K.; Sakakura, C.; Fukamachi, H.; Inoue, K.; Chi, X.-Z.; Lee, K.-Y.; Nomura, S.; Lee, C.-W.; Han, S.-B.; Kim, H.-M.; Kim, W.-J.; and 15 others : Causal relationship between the loss of RUNX3 expression and gastric cancer. Cell 109: 113-124, 2002. ; and

[41449] Wijmenga, C.; Speck, N. A.; Dracopoli, N. C.; Hofker, M. H.; Liu, P.; Collins, F. S. : Identification of a new murine runt domain-containing gene, Cbfa3, and localization of the human h.

[41450] Further studies establishing the function and utilities of RUNX3 are found in John Hopkins OMIM database record ID 600210, and in cited publications numbered 1622-162 and 1630-1626 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence.SH3-domain Binding Protein 5 (BTK-associated) (SH3BP5, Accession NM_004844) is another VGAM1151 host target gene. SH3BP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP5 BINDING SITE, designated SEQ ID:11257, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41451] Another function of VGAM1151 is therefore inhibition of SH3-domain Binding Protein 5 (BTK-associated) (SH3BP5, Accession NM_004844), a gene which plays a negative regulatory role in btk-related cytoplasmic signaling in b cells. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP5. The function of SH3BP5 has been established by previous studies. Bruton tyrosine kinase (BTK; 300300) is a cytoplasmic tyrosine kinase crucial for the maturation of B-lineage cells. BTK deficiency is involved in the pathogenesis of X-linked immunodeficiency. By Far Western expression cloning using a human

placenta cDNA library for molecules associated with the SH3 domain of BTK, followed by screening brain and B-cell cDNA libraries, Matsushita et al. (1998) obtained a cDNA encoding SH3BP5, which they termed SAB (SH3 domain-binding protein that preferentially associates with BTK). SH3BP5 encodes a deduced 425-amino acid protein. Northern blot analysis revealed wide expression of a 3.0-kb transcript, with especially prominent expression in testis and ovary. Immunoblot analysis showed that SH3BP5 is expressed as a 70-kD protein. Immunoprecipitation analysis suggested that SH3BP5 interacts with BTK in cells. Mutational and immunoblot analyses showed that amino acids 163 to 193 of SH3BP5 bind most strongly to the SH3 domain of BTK and not with the SH3 domains of a number of other cytoplasmic tyrosine kinases. Using immunoprecipitation and functional analysis, Yamadori et al. (1999) demonstrated that SH3BP5 inhibits BTK activity by binding to the enzyme.

[41452] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41453] Matsushita, M.; Yamadori, T.; Kato, S.; Takemoto, Y.; Inazawa, J.; Baba, Y.; Hashimoto, S.; Sekine, S.; Arai, S.; Ku-

nikata, T.; Kurimoto, M.; Kishimoto, T.; Tsukada, S. : Identification and characterization of a novel SH3-domain binding protein, Sab, which preferentially associates with Bruton's tyrosine kinase (Btk). Biochem. Biophys. Res. Commun. 245: 337-343, 1998. ; and

[41454] Yamadori, T.; Baba, Y.; Matsushita, M.; Hashimoto, S.; Kurosaki, M.; Kurosaki, T.; Kishimoto, T.; Tsukada, S. : Bruton's tyrosine kinase activity is negatively regulated by Sab, the Btk-SH.

[41455] Further studies establishing the function and utilities of SH3BP5 are found in John Hopkins OMIM database record ID 605612, and in cited publications numbered 6772-677 and 6770 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. *Sine Oculis Homeobox Homolog 2 (Drosophila) (SIX2*, Accession NM_016932) is another VGAM1151 host target gene. SIX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIX2 BINDING SITE, designated SEQ ID:18850, to the nucleotide sequence of VGAM1151 RNA, herein

designated VGAM RNA, also designated SEQ ID:3862.

[41456] Another function of VGAM1151 is therefore inhibition of Sine Oculis Homeobox Homolog 2 (Drosophila) (SIX2, Accession NM_016932), a gene which may be involved in limb tendon and ligament development (by similarity). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIX2. The function of SIX2 has been established by previous studies. By screening a human genomic library with a human SIX1 cDNA (OMIM Ref. No. 601205), Boucher et al. (2000) identified the SIX2 gene. Using the SIX2 genomic sequence, they isolated a human fetus SIX2 cDNA. The predicted 291-amino acid SIX2 protein contains a SIX domain and a homeodomain. The human SIX2 protein is almost identical to the mouse Six2 protein. Northern blot analysis of human tissues detected strong expression of a major 2.2-kb SIX2 transcript in skeletal muscle, with weaker expression in pancreas. RT-PCR showed SIX2 expression in all human fetal tissues tested except lung. In adult tissues, RT-PCR revealed SIX2 expression in skeletal muscle, pancreas, ovary, and sclera; SIX2 expression was not detected in other regions of the adult eye and optic nerve or in adult heart, lung, kidney,

liver, or breast. Boucher et al. (2000) determined that the human SIX2 gene contains 2 exons.

[41457] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41458] Boucher, C. A.; Winchester, C. L.; Hamilton, G. M.; Winter, A. D.; Johnson, K. J.; Bailey, M. E. S. : Structure, mapping and expression of the human gene encoding the homeodomain protein, SIX2. Gene 247: 145–151, 2000. ; and

[41459] Oliver, G.; Wehr, R.; Jenkins, N. A.; Copeland, N. G.; Cheyette, B. N. R.; Hartenstein, V.; Zipursky, S. L.; Gruss, P. : Homeobox genes and connective tissue patterning. Development 12.

[41460] Further studies establishing the function and utilities of SIX2 are found in John Hopkins OMIM database record ID 604994, and in cited publications numbered 7101 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983) is another VGAM1151 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10129, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41461] Another function of VGAM1151 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87. Transducin (beta)-like 1X-linked (TBL1X, Accession NM_005647) is another VGAM1151 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BIND-

ING SITE, designated SEQ ID:12183, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41462] Another function of VGAM1151 is therefore inhibition of Transducin (beta)-like 1X-linked (TBL1X, Accession NM_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X has been established by previous studies. In the course of constructing a deletion map of the distal portion of the short arm of the X chromosome and the identification of the OA1 gene (OMIM Ref. No. 300500), Bassi et al. (1999) performed cDNA selection experiments that resulted in the isolation of a novel gene, TBL1, located outside the OA1 critical region on the telomeric side. The TBL1 gene maps to the Xp22.3 region and shares significant homology with members of the WD40 repeat-containing protein family. The open reading frame encodes a 526-amino acid protein containing 6 beta-transducin repeats (WD40 motif) in the C-terminal domain. The homology with known beta-subunits of G proteins and other WD40 repeat-containing proteins is restricted to the WD40 motif.

Northern blot analysis indicated that the TBL1 gene is ubiquitously expressed as 2 transcripts of approximately 2.1 and 6.0 kb. Matsuzawa and Reed (2001) elucidated a network of protein interactions in which SIAH1 (OMIM Ref. No. 602212), SIP (OMIM Ref. No. 606186), SKP1 (OMIM Ref. No. 601434), and EBI collaborate in a pathway controlling beta-catenin (OMIM Ref. No. 116806) levels, affecting activity of beta-catenin-dependent TCF (e.g., TCF1; 142410) and LEF (e.g., LEF1; 153245) transcription factors. This pathway is inducible by p53 (OMIM Ref. No. 191170), revealing a link between genotoxic injury responses and beta-catenin degradation. SIAH1 is physically linked to EBI by association with SIP, which binds SKP1.

[41463] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41464] Bassi, M. T.; Ramesar, R. S.; Caciotti, B.; Winship, I. M.; De Grandi, A.; Riboni, M.; Townes, P. L.; Beighton, P.; Ballabio, A.; Borsani, G. : X-linked late-onset sensorineural deafness caused by a deletion involving OA1 and a novel gene containing WD-40 repeats. Am. J. Hum. Genet. 64: 1604-1616, 1999. ; and

[41465] Matsuzawa, S.; Reed, J. C. : Siah-1, SIP, and Ebi collaborate

in a novel pathway for beta-catenin degradation linked to p53 responses. *Molec. Cell* 7: 915–926, 2001.

[41466] Further studies establishing the function and utilities of TBL1X are found in John Hopkins OMIM database record ID 300196, and in cited publications numbered 11395–11398, 725 and 11399–11400 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242) is another VGAM1151 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB2 BINDING SITE, designated SEQ ID:9239, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41467] Another function of VGAM1151 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

TGFB2. Tumor Necrosis Factor (ligand) Superfamily, Member 5 (hyper-IgM syndrome) (TNFSF5, Accession NM_000074) is another VGAM1151 host target gene. TNFSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF5 BINDING SITE, designated SEQ ID:5519, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41468] Another function of VGAM1151 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 5 (hyper-IgM syndrome) (TNFSF5, Accession NM_000074). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF5. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM1151 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15352, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41469] Another function of VGAM1151 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949) is another VGAM1151 host target gene. ACTR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1A BINDING SITE, designated SEQ ID:31535, to the

nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41470] Another function of VGAM1151 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR1A. BCL2-like 1 (BCL2L1, Accession NM_138578) is another VGAM1151 host target gene. BCL2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L1 BINDING SITE, designated SEQ ID:28893, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41471] Another function of VGAM1151 is therefore inhibition of BCL2-like 1 (BCL2L1, Accession NM_138578). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L1. Baculoviral IAP Repeat-containing 5

(survivin) (BIRC5, Accession NM_001168) is another VGAM1151 host target gene. BIRC5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BIRC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC5 BINDING SITE, designated SEQ ID:6836, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41472] Another function of VGAM1151 is therefore inhibition of Baculoviral IAP Repeat-containing 5 (survivin) (BIRC5, Accession NM_001168). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC5. Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072) is another VGAM1151 host target gene. C1QR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1QR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QR1 BINDING SITE, des-

ignated SEQ ID:14333, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41473] Another function of VGAM1151 is therefore inhibition of Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QR1. Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749) is another VGAM1151 host target gene. C20orf139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf139 BINDING SITE, designated SEQ ID:41105, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41474] Another function of VGAM1151 is therefore inhibition of Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with C20orf139. Chromosome 6 Open Reading Frame 9 (C6orf9, Accession NM_022107) is another VGAM1151 host target gene. C6orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf9 BINDING SITE, designated SEQ ID:22656, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41475] Another function of VGAM1151 is therefore inhibition of Chromosome 6 Open Reading Frame 9 (C6orf9, Accession NM_022107). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf9. CRK7 (Accession NM_016507) is another VGAM1151 host target gene. CRK7 BINDING SITE1 and CRK7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CRK7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of CRK7 BINDING SITE1 and CRK7 BINDING SITE2, designated SEQ ID:18586 and SEQ ID:18585 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41476] Another function of VGAM1151 is therefore inhibition of CRK7 (Accession NM_016507). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRK7. DCMF Deaminase (DCTD, Accession NM_001921) is another VGAM1151 host target gene. DCTD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCTD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCTD BINDING SITE, designated SEQ ID:7637, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41477] Another function of VGAM1151 is therefore inhibition of DCMF Deaminase (DCTD, Accession NM_001921). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with DCTD. FLJ12572 (Accession NM_022905) is another VGAM1151 host target gene. FLJ12572 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23202, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41478] Another function of VGAM1151 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. FLJ13154 (Accession NM_024598) is another VGAM1151 host target gene. FLJ13154 BINDING SITE1 through FLJ13154 BINDING SITE9 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ13154, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13154 BINDING SITE1 through FLJ13154 BINDING SITE9, designated SEQ ID:23837, SEQ

ID:23838, SEQ ID:23839, SEQ ID:23840, SEQ ID:23841, SEQ ID:23842, SEQ ID:23843, SEQ ID:23845 and SEQ ID:23846 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41479] Another function of VGAM1151 is therefore inhibition of FLJ13154 (Accession NM_024598). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13154. FLJ22671 (Accession NM_024861) is another VGAM1151 host target gene. FLJ22671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22671 BINDING SITE, designated SEQ ID:24295, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41480] Another function of VGAM1151 is therefore inhibition of FLJ22671 (Accession NM_024861). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22671. FLJ22679 (Accession NM_017698) is another VGAM1151 host target gene. FLJ22679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22679 BINDING SITE, designated SEQ ID:19262, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41481] Another function of VGAM1151 is therefore inhibition of FLJ22679 (Accession NM_017698). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22679. FLJ23263 (Accession NM_025115) is another VGAM1151 host target gene. FLJ23263 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23263 BINDING SITE, designated SEQ ID:24766, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM

RNA, also designated SEQ ID:3862.

[41482] Another function of VGAM1151 is therefore inhibition of FLJ23263 (Accession NM_025115). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23263. FLJ30574 (Accession NM_144629) is another VGAM1151 host target gene. FLJ30574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30574 BINDING SITE, designated SEQ ID:29448, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41483] Another function of VGAM1151 is therefore inhibition of FLJ30574 (Accession NM_144629). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30574. HSPC065 (Accession NM_014157) is another VGAM1151 host target gene. HSPC065 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC065, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15452, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41484] Another function of VGAM1151 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. HIV TAT Specific Factor 1 (HTATSF1, Accession NM_014500) is another VGAM1151 host target gene. HTATSF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTATSF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTATSF1 BINDING SITE, designated SEQ ID:15837, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41485] Another function of VGAM1151 is therefore inhibition of HIV TAT Specific Factor 1 (HTATSF1, Accession

NM_014500). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTATSF1. JIK (Accession NM_016281) is another VGAM1151 host target gene. JIK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JIK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JIK BINDING SITE, designated SEQ ID:18408, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41486] Another function of VGAM1151 is therefore inhibition of JIK (Accession NM_016281). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JIK. KIAA0210 (Accession NM_014744) is another VGAM1151 host target gene. KIAA0210 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0210 BINDING SITE,

designated SEQ ID:16423, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41487] Another function of VGAM1151 is therefore inhibition of KIAA0210 (Accession NM_014744). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0210. KIAA0450 (Accession NM_014638) is another VGAM1151 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated SEQ ID:16032, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41488] Another function of VGAM1151 is therefore inhibition of KIAA0450 (Accession NM_014638). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA0721 (Accession NM_021648) is another VGAM1151 host target gene. KIAA0721 BINDING SITE1

and KIAA0721 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0721, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0721 BINDING SITE1 and KIAA0721 BINDING SITE2, designated SEQ ID:22319 and SEQ ID:45926 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41489] Another function of VGAM1151 is therefore inhibition of KIAA0721 (Accession NM_021648). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0721. KIAA1029 (Accession NM_007286) is another VGAM1151 host target gene. KIAA1029 BINDING SITE1 and KIAA1029 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1029, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1029 BINDING SITE1 and KIAA1029 BINDING SITE2, designated SEQ ID:14145 and SEQ

ID:32639 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41490] Another function of VGAM1151 is therefore inhibition of KIAA1029 (Accession NM_007286). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1029. KIAA1384 (Accession XM_035405) is another VGAM1151 host target gene. KIAA1384 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1384, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1384 BINDING SITE, designated SEQ ID:32259, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41491] Another function of VGAM1151 is therefore inhibition of KIAA1384 (Accession XM_035405). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1384. MGC10765 (Accession NM_024345) is another VGAM1151 host target gene. MGC10765 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10765 BINDING SITE, designated SEQ ID:23644, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41492] Another function of VGAM1151 is therefore inhibition of MGC10765 (Accession NM_024345). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10765. MGC10812 (Accession NM_031425) is another VGAM1151 host target gene. MGC10812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10812 BINDING SITE, designated SEQ ID:25410, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41493] Another function of VGAM1151 is therefore inhibition of

MGC10812 (Accession NM_031425). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10812. MGC11115 (Accession NM_032310) is another VGAM1151 host target gene. MGC11115 BINDING SITE1 and MGC11115 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC11115, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11115 BINDING SITE1 and MGC11115 BINDING SITE2, designated SEQ ID:26094 and SEQ ID:26095 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41494] Another function of VGAM1151 is therefore inhibition of MGC11115 (Accession NM_032310). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11115. MGC13053 (Accession NM_032710) is another VGAM1151 host target gene. MGC13053 BINDING SITE1 and MGC13053 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA en-

coded by MGC13053, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13053 BINDING SITE1 and MGC13053 BINDING SITE2, designated SEQ ID:26424 and SEQ ID:27938 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41495] Another function of VGAM1151 is therefore inhibition of MGC13053 (Accession NM_032710). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13053. MGC4796 (Accession XM_029031) is another VGAM1151 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30835, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41496] Another function of VGAM1151 is therefore inhibition of

MGC4796 (Accession XM_029031). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. MOST2 (Accession NM_020250) is another VGAM1151 host target gene. MOST2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOST2 BINDING SITE, designated SEQ ID:21552, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41497] Another function of VGAM1151 is therefore inhibition of MOST2 (Accession NM_020250). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOST2. NPD009 (Accession XM_170795) is another VGAM1151 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of NPD009 BINDING SITE, designated SEQ ID:45564, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41498] Another function of VGAM1151 is therefore inhibition of NPD009 (Accession XM_170795). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Neuritin 1 (NRN1, Accession NM_016588) is another VGAM1151 host target gene. NRN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRN1 BINDING SITE, designated SEQ ID:18664, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41499] Another function of VGAM1151 is therefore inhibition of Neuritin 1 (NRN1, Accession NM_016588). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRN1. Olfactory Receptor, Family 7, Subfamily C,

Member 1 (OR7C1, Accession NM_017506) is another VGAM1151 host target gene. OR7C1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OR7C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OR7C1 BINDING SITE, designated SEQ ID:18962, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41500] Another function of VGAM1151 is therefore inhibition of Olfactory Receptor, Family 7, Subfamily C, Member 1 (OR7C1, Accession NM_017506). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OR7C1. PFTK1 Protein Kinase 1 (PFTK1, Accession NM_012395) is another VGAM1151 host target gene. PFTK1 BINDING SITE1 and PFTK1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PFTK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFTK1 BINDING SITE1 and PFTK1 BINDING

SITE2, designated SEQ ID:14752 and SEQ ID:14753 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41501] Another function of VGAM1151 is therefore inhibition of PFTAIK Protein Kinase 1 (PFTK1, Accession NM_012395). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFTK1. Regulatory Factor X, 3 (influences HLA class II expression) (RFX3, Accession NM_134428) is another VGAM1151 host target gene. RFX3 BINDING SITE1 and RFX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RFX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX3 BINDING SITE1 and RFX3 BINDING SITE2, designated SEQ ID:28670 and SEQ ID:8828 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41502] Another function of VGAM1151 is therefore inhibition of Regulatory Factor X, 3 (influences HLA class II expression)

(RFX3, Accession NM_134428). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX3. Tripartite Motif-containing 15 (TRIM15, Accession NM_033229) is another VGAM1151 host target gene. TRIM15 BINDING SITE1 and TRIM15 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM15, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM15 BINDING SITE1 and TRIM15 BINDING SITE2, designated SEQ ID:27074 and SEQ ID:27075 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41503] Another function of VGAM1151 is therefore inhibition of Tripartite Motif-containing 15 (TRIM15, Accession NM_033229). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM15. LOC112868 (Accession XM_053402) is another VGAM1151 host target gene. LOC112868 BINDING SITE1 through LOC112868 BINDING SITE4 are HOST TARGET binding sites found in

untranslated regions of mRNA encoded by LOC112868, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112868 BINDING SITE1 through LOC112868 BINDING SITE4, designated SEQ ID:36080, SEQ ID:36081, SEQ ID:36086 and SEQ ID:36087 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41504] Another function of VGAM1151 is therefore inhibition of LOC112868 (Accession XM_053402). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112868. LOC113612 (Accession XM_054492) is another VGAM1151 host target gene. LOC113612 BINDING SITE1 and LOC113612 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC113612, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113612 BINDING SITE1 and LOC113612 BINDING SITE2, designated SEQ ID:36170

and SEQ ID:36570 respectively, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41505] Another function of VGAM1151 is therefore inhibition of LOC113612 (Accession XM_054492). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113612. LOC131034 (Accession NM_130808) is another VGAM1151 host target gene. LOC131034 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC131034, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131034 BINDING SITE, designated SEQ ID:28316, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41506] Another function of VGAM1151 is therefore inhibition of LOC131034 (Accession NM_130808). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131034. LOC144231 (Accession XM_096561) is another VGAM1151 host target gene. LOC144231 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144231 BINDING SITE, designated SEQ ID:40392, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41507] Another function of VGAM1151 is therefore inhibition of LOC144231 (Accession XM_096561). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144231. LOC144262 (Accession XM_084793) is another VGAM1151 host target gene. LOC144262 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144262 BINDING SITE, designated SEQ ID:37704, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41508] Another function of VGAM1151 is therefore inhibition of

LOC144262 (Accession XM_084793). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144262. LOC146839 (Accession XM_097107) is another VGAM1151 host target gene. LOC146839 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146839 BINDING SITE, designated SEQ ID:40754, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41509] Another function of VGAM1151 is therefore inhibition of LOC146839 (Accession XM_097107). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146839. LOC150577 (Accession XM_097918) is another VGAM1151 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41221, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41510] Another function of VGAM1151 is therefore inhibition of LOC150577 (Accession XM_097918). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150577. LOC151742 (Accession NM_139245) is another VGAM1151 host target gene. LOC151742 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151742 BINDING SITE, designated SEQ ID:29243, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41511] Another function of VGAM1151 is therefore inhibition of LOC151742 (Accession NM_139245). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151742. LOC154761 (Accession XM_088038) is an-

other VGAM1151 host target gene. LOC154761 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154761 BINDING SITE, designated SEQ ID:39484, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41512] Another function of VGAM1151 is therefore inhibition of LOC154761 (Accession XM_088038). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154761. LOC201617 (Accession XM_117315) is another VGAM1151 host target gene. LOC201617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201617 BINDING SITE, designated SEQ ID:43381, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41513] Another function of VGAM1151 is therefore inhibition of LOC201617 (Accession XM_117315). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201617. LOC201799 (Accession XM_114380) is another VGAM1151 host target gene. LOC201799 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201799, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201799 BINDING SITE, designated SEQ ID:42917, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41514] Another function of VGAM1151 is therefore inhibition of LOC201799 (Accession XM_114380). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201799. LOC221477 (Accession XM_166397) is another VGAM1151 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44261, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41515] Another function of VGAM1151 is therefore inhibition of LOC221477 (Accession XM_166397). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC221662 (Accession XM_166466) is another VGAM1151 host target gene. LOC221662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221662 BINDING SITE, designated SEQ ID:44388, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41516] Another function of VGAM1151 is therefore inhibition of LOC221662 (Accession XM_166466). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221662. LOC253847 (Accession XM_171145) is another VGAM1151 host target gene. LOC253847 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253847, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253847 BINDING SITE, designated SEQ ID:45940, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41517] Another function of VGAM1151 is therefore inhibition of LOC253847 (Accession XM_171145). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253847. LOC254945 (Accession XM_173038) is another VGAM1151 host target gene. LOC254945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254945 BINDING SITE, designated SEQ ID:46305, to the nucleotide sequence of VGAM1151 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3862.

[41518] Another function of VGAM1151 is therefore inhibition of LOC254945 (Accession XM_173038). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254945. LOC51008 (Accession NM_015947) is another VGAM1151 host target gene. LOC51008 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51008 BINDING SITE, designated SEQ ID:18063, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41519] Another function of VGAM1151 is therefore inhibition of LOC51008 (Accession NM_015947). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51008. LOC56930 (Accession XM_030603) is another VGAM1151 host target gene. LOC56930 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56930, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56930 BINDING SITE, designated SEQ ID:31092, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41520] Another function of VGAM1151 is therefore inhibition of LOC56930 (Accession XM_030603). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56930. LOC91812 (Accession XM_040857) is another VGAM1151 host target gene. LOC91812 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91812 BINDING SITE, designated SEQ ID:33392, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41521] Another function of VGAM1151 is therefore inhibition of LOC91812 (Accession XM_040857). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91812. LOC91813 (Accession XM_040862) is another VGAM1151 host target gene. LOC91813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE, designated SEQ ID:33400, to the nucleotide sequence of VGAM1151 RNA, herein designated VGAM RNA, also designated SEQ ID:3862.

[41522] Another function of VGAM1151 is therefore inhibition of LOC91813 (Accession XM_040862). Accordingly, utilities of VGAM1151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1152 (VGAM1152) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41523] VGAM1152 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1152 was detected is described hereinabove with reference to Figs. 1–8.

[41524] VGAM1152 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41525] VGAM1152 gene encodes a VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1152 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1152 precursor RNA is designated SEQ ID:1138, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1138 is located at position 4584 relative to the genome of Cowpox Virus.

[41526] VGAM1152 precursor RNA folds onto itself, forming VGAM1152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41527] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1152 folded precursor RNA into VGAM1152 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1152 RNA is designated SEQ ID:3863, and is provided hereinbelow with reference to the sequence listing part.

[41528] VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1152 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41529] VGAM1152 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1152 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1152 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41530] The complementary binding of VGAM1152 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1152 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1152 host target RNA into VGAM1152 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41531] It is appreciated that VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1152 host target genes. The mRNA of each one of this plurality of VGAM1152 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1152 RNA, herein designated VGAM RNA, and which when bound by VGAM1152 RNA causes inhibition of translation of respective one or more VGAM1152 host target proteins.

[41532] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1152 gene, herein designated VGAM GENE, on one or more VGAM1152 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41533] It is yet further appreciated that a function of VGAM1152 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1152 correlate with, and may be deduced from, the identity of the host target genes which VGAM1152 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41534] Nucleotide sequences of the VGAM1152 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1152 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1152 are further described hereinbelow with reference to Table 1.

[41535] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1152 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1152 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41536] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1152 gene, herein designated VGAM is inhibition of expression of VGAM1152 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1152 correlate with, and may be deduced from, the identity of the target genes which VGAM1152 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41537] EphA3 (EPHA3, Accession NM_005233) is a VGAM1152 host target gene. EPHA3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by EPHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA3 BINDING SITE, designated SEQ ID:11743, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41538] A function of VGAM1152 is therefore inhibition of EphA3 (EPHA3, Accession NM_005233), a gene which binds to ephrin-a2, -a3, -a4 and -a5. could play a role in lymphoid function. Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA3. The function of EPHA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164. Gamma-aminobutyric Acid (GABA) A Receptor, Pi (GABRP, Accession NM_014211) is another VGAM1152 host target gene. GABRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GABRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of GABRP BINDING SITE, designated SEQ ID:15479, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41539] Another function of VGAM1152 is therefore inhibition of Gamma-aminobutyric Acid (GABA) A Receptor, ρ 1 (GABRP, Accession NM_014211), a gene which mediates neuronal inhibition by binding to the gaba/benzodiazepine receptor and opening an integral chloride channel. Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABRP. The function of GABRP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Tuftelin 1 (TUFT1, Accession NM_020127) is another VGAM1152 host target gene. TUFT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUFT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUFT1 BINDING SITE, designated SEQ ID:21318, to the nucleotide sequence of VGAM1152 RNA,

herein designated VGAM RNA, also designated SEQ ID:3863.

[41540] Another function of VGAM1152 is therefore inhibition of Tuftelin 1 (TUFT1, Accession NM_020127), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUFT1. The function of TUFT1 has been established by previous studies. Tuftelin is an acidic protein found in developing and mature extracellular enamel, the unique and highly mineralized ectodermal tissue covering vertebrate teeth (Deutsch, 1989; Deutsch et al., 1991). It is thought to play a major role in mineralization and structural organization of enamel. By fluorescence in situ hybridization, Deutsch et al. (1994) mapped the TUFT1 gene to 1q21-q31. They raised the possibility that an autosomal dominant form of amelogenesis imperfecta (104500, 104530) is due to a mutation in this gene. By FISH, Bashir et al. (1998) localized the TUFT1 gene to 1q21.

[41541] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [41542] Deutsch, D.; Palmon, A.; Fisher, L. W.; Kolodny, N.; Termine, J. D.; Young, M. F. : Sequencing of bovine enamelin (tuftelin), a novel acidic enamel protein. J. Biol. Chem. 266: 16021–16028, 1991. ; and
- [41543] Deutsch, D.; Palmon, A.; Young, M. F.; Selig, S.; Kearns, W. G.; Fisher, L. W. : Mapping of the human tuftelin (TUFT1) gene to chromosome 1 by fluorescence in situ hybridization. (Abstrac.
- [41544] Further studies establishing the function and utilities of TUFT1 are found in John Hopkins OMIM database record ID 600087, and in cited publications numbered 7900–7901, 821 and 8224–8226 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ABLIM (Accession NM_006720) is another VGAM1152 host target gene. ABLIM BINDING SITE1 and ABLIM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABLIM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABLIM BINDING SITE1 and ABLIM BINDING SITE2, designated SEQ ID:13550 and SEQ ID:8117 respec–

tively, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41545] Another function of VGAM1152 is therefore inhibition of ABLIM (Accession NM_006720). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABLIM. KIAA0565 (Accession XM_039912) is another VGAM1152 host target gene. KIAA0565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0565 BINDING SITE, designated SEQ ID:33220, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41546] Another function of VGAM1152 is therefore inhibition of KIAA0565 (Accession XM_039912). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0565. KIAA0635 (Accession NM_014645) is another VGAM1152 host target gene. KIAA0635 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0635 BINDING SITE, designated SEQ ID:16054, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41547] Another function of VGAM1152 is therefore inhibition of KIAA0635 (Accession NM_014645). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0635. MacGAP (Accession NM_033515) is another VGAM1152 host target gene. MacGAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MacGAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MacGAP BINDING SITE, designated SEQ ID:27289, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41548] Another function of VGAM1152 is therefore inhibition of

MacGAP (Accession NM_033515). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MacGAP. MGC13130 (Accession NM_032890) is another VGAM1152 host target gene. MGC13130 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13130 BINDING SITE, designated SEQ ID:26713, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41549] Another function of VGAM1152 is therefore inhibition of MGC13130 (Accession NM_032890). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13130. LOC131368 (Accession XM_067347) is another VGAM1152 host target gene. LOC131368 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC131368 BINDING SITE, designated SEQ ID:37355, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41550] Another function of VGAM1152 is therefore inhibition of LOC131368 (Accession XM_067347). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131368. LOC153077 (Accession XM_098307) is another VGAM1152 host target gene. LOC153077 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153077 BINDING SITE, designated SEQ ID:41569, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41551] Another function of VGAM1152 is therefore inhibition of LOC153077 (Accession XM_098307). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153077. LOC256207 (Accession XM_170837) is an-

other VGAM1152 host target gene. LOC256207 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256207, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256207 BINDING SITE, designated SEQ ID:45621, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41552] Another function of VGAM1152 is therefore inhibition of LOC256207 (Accession XM_170837). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256207. LOC90288 (Accession XM_030669) is another VGAM1152 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31112, to the nucleotide sequence of VGAM1152 RNA, herein designated VGAM RNA, also designated SEQ ID:3863.

[41553] Another function of VGAM1152 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities of VGAM1152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1153 (VGAM1153) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41554] VGAM1153 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1153 was detected is described hereinabove with reference to Figs. 1–8.

[41555] VGAM1153 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41556] VGAM1153 gene encodes a VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1153 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1153 precursor RNA is designated SEQ ID:1139, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1139 is located at position 2676 relative to the genome of Cowpox Virus.

[41557] VGAM1153 precursor RNA folds onto itself, forming VGAM1153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41558] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1153 folded precursor RNA into VGAM1153 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1153 RNA is designated SEQ ID:3864, and is provided hereinbelow with reference to the sequence listing part.

[41559] VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1153 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[41560] VGAM1153 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1153 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1153 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41561] The complementary binding of VGAM1153 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1153 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1153 host target RNA into VGAM1153 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41562] It is appreciated that VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1153 host target genes. The mRNA of each one of this plurality of VGAM1153 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1153 RNA, herein designated VGAM RNA, and which when bound by VGAM1153 RNA causes inhibition of translation of respective one or more VGAM1153 host target proteins.

[41563] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1153 gene, herein designated VGAM GENE, on one or more VGAM1153 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41564] It is yet further appreciated that a function of VGAM1153 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1153 correlate with, and may be deduced from, the identity of the host target genes which VGAM1153 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41565] Nucleotide sequences of the VGAM1153 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1153 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1153 are further described hereinbelow with reference to Table 1.

[41566] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1153 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1153 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[41567] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1153 gene, herein designated VGAM is inhibition of expression of VGAM1153 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1153 correlate with, and may be deduced from, the identity of the target genes which VGAM1153 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41568] Ac-like Transposable Element (ALTE, Accession NM_004729) is a VGAM1153 host target gene. ALTE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALTE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALTE BINDING SITE, designated SEQ ID:11107, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, also designated SEQ ID:3864.

[41569] A function of VGAM1153 is therefore inhibition of Ac-like Transposable Element (ALTE, Accession NM_004729). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with ALTE. FLJ23598 (Accession NM_024783) is another VGAM1153 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24158, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, also designated SEQ ID:3864.

[41570] Another function of VGAM1153 is therefore inhibition of FLJ23598 (Accession NM_024783). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. HMP19 (Accession XM_113455) is another VGAM1153 host target gene. HMP19 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HMP19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMP19 BINDING SITE, designated SEQ ID:42273, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA,

also designated SEQ ID:3864.

[41571] Another function of VGAM1153 is therefore inhibition of HMP19 (Accession XM_113455). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMP19. KIAA1710 (Accession XM_031283) is another VGAM1153 host target gene. KIAA1710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1710 BINDING SITE, designated SEQ ID:31332, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, also designated SEQ ID:3864.

[41572] Another function of VGAM1153 is therefore inhibition of KIAA1710 (Accession XM_031283). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1710. LOC143943 (Accession XM_096504) is another VGAM1153 host target gene. LOC143943 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143943, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143943 BINDING SITE, designated SEQ ID:40384, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, also designated SEQ ID:3864.

[41573] Another function of VGAM1153 is therefore inhibition of LOC143943 (Accession XM_096504). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143943. LOC58489 (Accession XM_051862) is another VGAM1153 host target gene. LOC58489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC58489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC58489 BINDING SITE, designated SEQ ID:35905, to the nucleotide sequence of VGAM1153 RNA, herein designated VGAM RNA, also designated SEQ ID:3864.

[41574] Another function of VGAM1153 is therefore inhibition of LOC58489 (Accession XM_051862). Accordingly, utilities of VGAM1153 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC58489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1154 (VGAM1154) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41575] VGAM1154 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1154 was detected is described hereinabove with reference to Figs. 1–8.

[41576] VGAM1154 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41577] VGAM1154 gene encodes a VGAM1154 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1154 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1154 precursor RNA is desig-

nated SEQ ID:1140, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1140 is located at position 1704 relative to the genome of Cowpox Virus.

- [41578] VGAM1154 precursor RNA folds onto itself, forming VGAM1154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [41579] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1154 folded precursor RNA into VGAM1154 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1154 RNA is designated SEQ ID:3865, and is provided hereinbelow with reference to the sequence

listing part.

[41580] VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1154 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41581] VGAM1154 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1154 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1154 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41582] The complementary binding of VGAM1154 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1154 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1154 host target RNA into VGAM1154 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41583] It is appreciated that VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1154 host target genes. The mRNA of each one of this plurality of VGAM1154 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1154 RNA, herein designated VGAM

RNA, and which when bound by VGAM1154 RNA causes inhibition of translation of respective one or more VGAM1154 host target proteins.

[41584] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1154 gene, herein designated VGAM GENE, on one or more VGAM1154 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41585] It is yet further appreciated that a function of VGAM1154 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1154 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1154 correlate with, and may be deduced from, the identity of the host target genes which VGAM1154 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41586] Nucleotide sequences of the VGAM1154 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1154 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1154 are further described hereinbelow with reference to Table 1.

[41587] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1154 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1154 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41588] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1154 gene, herein designated VGAM is

inhibition of expression of VGAM1154 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1154 correlate with, and may be deduced from, the identity of the target genes which VGAM1154 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41589] Cyclic Nucleotide Gated Channel Beta 3 (CNGB3, Accession NM_019098) is a VGAM1154 host target gene. CNGB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNGB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNGB3 BINDING SITE, designated SEQ ID:21175, to the nucleotide sequence of VGAM1154 RNA, herein designated VGAM RNA, also designated SEQ ID:3865.

[41590] A function of VGAM1154 is therefore inhibition of Cyclic Nucleotide Gated Channel Beta 3 (CNGB3, Accession NM_019098). Accordingly, utilities of VGAM1154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNGB3. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM1154 host target gene. CALN1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25517, to the nucleotide sequence of VGAM1154 RNA, herein designated VGAM RNA, also designated SEQ ID:3865.

[41591] Another function of VGAM1154 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM1154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1155 (VGAM1155) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41592] VGAM1155 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1155 was detected is described hereinabove with reference to Figs. 1-8.

[41593] VGAM1155 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus.

VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41594] VGAM1155 gene encodes a VGAM1155 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1155 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1155 precursor RNA is designated SEQ ID:1141, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1141 is located at position 147349 relative to the genome of Cowpox Virus.

[41595] VGAM1155 precursor RNA folds onto itself, forming VGAM1155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[41596] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1155 folded precursor RNA into VGAM1155 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1155 RNA is designated SEQ ID:3866, and is provided hereinbelow with reference to the sequence listing part.

[41597] VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1155 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41598] VGAM1155 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1155 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1155 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1155 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41599] The complementary binding of VGAM1155 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1155 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1155 host target RNA into VGAM1155 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41600] It is appreciated that VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1155 host target genes. The mRNA of each one of this plurality of VGAM1155 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1155 RNA, herein designated VGAM RNA, and which when bound by VGAM1155 RNA causes inhibition of translation of respective one or more VGAM1155 host target proteins.

[41601] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1155 gene, herein designated VGAM GENE, on one or more VGAM1155 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41602] It is yet further appreciated that a function of VGAM1155 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1155 correlate with, and may be deduced from, the identity of the host target genes which VGAM1155 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41603] Nucleotide sequences of the VGAM1155 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1155 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1155 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1155 are further described hereinbelow with reference to Table 1.

[41604] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1155 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1155 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41605] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1155 gene, herein designated VGAM is inhibition of expression of VGAM1155 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1155 correlate with, and may be deduced from, the identity of the target genes which VGAM1155 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41606] Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858) is a VGAM1155 host target gene. COL19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of COL19A1 BINDING SITE, designated SEQ ID:7594, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41607] A function of VGAM1155 is therefore inhibition of Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858), a gene which may act as a cross-bridge between fibrils and other extracellular matrix molecules. Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL19A1. The function of COL19A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM19.ErbB2 Interacting Protein (ERBB2IP, Accession NM_018695) is another VGAM1155 host target gene. ERBB2IP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ERBB2IP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERBB2IP BINDING SITE, designated SEQ ID:20774, to the nucleotide

sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41608] Another function of VGAM1155 is therefore inhibition of Erbb2 Interacting Protein (ERBB2IP, Accession NM_018695), a gene which ERBB2 interacting protein; acts as an adaptor for the receptor ERBB2/HER2. Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERBB2IP. The function of ERBB2IP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1019. Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410) is another VGAM1155 host target gene. MGAT5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT5 BINDING SITE, designated SEQ ID:8239, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ

ID:3866.

[41609] Another function of VGAM1155 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT5. Retinoid X Receptor, Beta (RXRB, Accession NM_021976) is another VGAM1155 host target gene. RXRB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RXRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RXRB BINDING SITE, designated SEQ ID:22501, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41610] Another function of VGAM1155 is therefore inhibition of Retinoid X Receptor, Beta (RXRB, Accession NM_021976), a gene which binds to and serves as transcriptional coactivator for retinoic acid. Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RXRB. The function

of RXRB has been established by previous studies. The retinoic acid receptors, alpha (RARA; 180240), beta (RARB; 180220), and gamma (RARG; 180190), require coregulators to bind effectively to response elements and target genes. By a strategy of sequential screening of expression libraries with a retinoic acid response element and RAR, Yu et al. (1991) identified a cDNA encoding a coregulator highly related to RXR-alpha (OMIM Ref. No. 180245). This protein, termed RXR-beta, formed heterodimers with RAR, preferentially increasing its DNA binding and transcriptional activity on promoters containing retinoic acid, but not thyroid hormone or vitamin D, response elements. Remarkably, RXR-beta also heterodimerized with thyroid hormone and vitamin D receptors, increasing both DNA binding and transcriptional function on their respective response elements. RXR-alpha also formed heterodimers with these receptors. These observations suggested that retinoid X receptors meet the criteria for biochemically characterized cellular coregulators and serve to target selectively the high affinity binding of retinoic acid, thyroid hormone, and vitamin D receptors to their cognate DNA response elements. In an elegant series of experiments designed to understand the effect of RXR activation on

cholesterol balance, Repa et al. (2000) treated animals with the rexinoid LG268. Animals treated with rexinoid exhibited marked changes in cholesterol balance, including inhibition of cholesterol absorption and repressed bile acid synthesis. Studies with receptor-selective agonists revealed that oxysterol receptors (LXRs, OMIM Ref. No. 602423 and 600380) and the bile acid receptor, FXR (OMIM Ref. No. 603826), are the RXR heterodimeric partners that mediate these effects by regulating expression of the reverse-cholesterol transporter, ABC1 (OMIM Ref. No. 600046), and the rate-limiting enzyme of bile acid synthesis, CYP7A1 (OMIM Ref. No. 118455), respectively. These RXR heterodimers serve as key regulators in cholesterol homeostasis by governing reverse cholesterol transport from peripheral tissues, bile acid synthesis in liver, and cholesterol absorption in intestine. Activation of RXR/LXR heterodimers inhibits cholesterol absorption by upregulation of ABC1 expression in the small intestine. Activation of RXR/FXR heterodimers represses CYP7A1 expression and bile acid production, leading to a failure to solubilize and absorb cholesterol. Studies have shown that RXR/FXR-mediated repression of CYP7A1 is dominant over RXR/LXR-mediated induction of CYP7A1, which ex-

plains why the rexinoid represses rather than activates CYP7A1 (Lu et al., 2000). Activation of the LXR signaling pathway results in the upregulation of ABC1 in peripheral cells, including macrophages, to efflux free cholesterol for transport back to the liver through high density lipoprotein, where it is converted to bile acids by the LXR-mediated increase in CYP7A1 expression. Secretion of biliary cholesterol in the presence of increased bile acid pools normally results in enhanced reabsorption of cholesterol; however, with the increased expression of ABC1 and efflux of cholesterol back into the lumen, there is a reduction in cholesterol absorption and net excretion of cholesterol and bile acid. Rexinoids therefore offer a novel class of agents for treating elevated cholesterol

[41611] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41612] Lu, T. T.; Makishima, M.; Repa, J. J.; Schoonjans, K.; Kerr, T. A.; Auwerx, J.; Mangelsdorf, D. J. : Molecular basis for feedback regulation of bile acid synthesis by nuclear receptors. *Molec. Cell* 6: 507–515, 2000. ; and

[41613] Repa, J. J.; Turley, S. D.; Lobaccaro, J.-M. A.; Medina, J.; Li, L.; Lustig, K.; Shan, B.; Heyman, R. A.; Dletschy, J. M.;

Mangelsdorf, D. J. : Regulation of absorption and ABC1-mediate.

[41614] Further studies establishing the function and utilities of RXRB are found in John Hopkins OMIM database record ID 180246, and in cited publications numbered 2726, 5949–5950, 5938, 5941, 595 and 5952 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ23598 (Accession NM_024783) is another VGAM1155 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24153, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41615] Another function of VGAM1155 is therefore inhibition of FLJ23598 (Accession NM_024783). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. KIAA1128 (Accession XM_043596) is another VGAM1155 host target gene. KIAA1128 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33965, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41616] Another function of VGAM1155 is therefore inhibition of KIAA1128 (Accession XM_043596). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1128. Kelch-like 6 (*Drosophila*) (KLHL6, Accession NM_130446) is another VGAM1155 host target gene. KLHL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL6 BINDING SITE, designated SEQ ID:28209, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41617] Another function of VGAM1155 is therefore inhibition of Kelch-like 6 (*Drosophila*) (KLHL6, Accession NM_130446). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL6. MGC10966 (Accession NM_031471) is another VGAM1155 host target gene. MGC10966 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10966 BINDING SITE, designated SEQ ID:25535, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41618] Another function of VGAM1155 is therefore inhibition of MGC10966 (Accession NM_031471). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10966. MGC15873 (Accession NM_032920) is another VGAM1155 host target gene. MGC15873 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15873, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15873 BINDING SITE, designated SEQ ID:26742, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41619] Another function of VGAM1155 is therefore inhibition of MGC15873 (Accession NM_032920). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15873. Platelet Derived Growth Factor C (PDGFC, Accession NM_016205) is another VGAM1155 host target gene. PDGFC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFC BINDING SITE, designated SEQ ID:18301, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41620] Another function of VGAM1155 is therefore inhibition of Platelet Derived Growth Factor C (PDGFC, Accession

NM_016205). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFC. POPX1 (Accession NM_014906) is another VGAM1155 host target gene. POPX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POPX1 BINDING SITE, designated SEQ ID:17121, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41621] Another function of VGAM1155 is therefore inhibition of POPX1 (Accession NM_014906). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POPX1. SAM Domain and HD Domain 1 (SAMHD1, Accession XM_028704) is another VGAM1155 host target gene. SAMHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SAMHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SAMHD1 BINDING SITE, designated SEQ ID:30733, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41622] Another function of VGAM1155 is therefore inhibition of SAM Domain and HD Domain 1 (SAMHD1, Accession XM_028704). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAMHD1. SCYD1 (Accession XM_165650) is another VGAM1155 host target gene. SCYD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYD1 BINDING SITE, designated SEQ ID:43711, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41623] Another function of VGAM1155 is therefore inhibition of SCYD1 (Accession XM_165650). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SCYD1. Sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase) (SIAT9, Accession NM_003896) is another VGAM1155 host target gene. SIAT9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SIAT9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT9 BINDING SITE, designated SEQ ID:9976, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41624] Another function of VGAM1155 is therefore inhibition of Sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase) (SIAT9, Accession NM_003896). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT9. LOC127534 (Accession XM_060532) is another VGAM1155 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37171, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41625] Another function of VGAM1155 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC130535 (Accession XM_072244) is another VGAM1155 host target gene. LOC130535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130535 BINDING SITE, designated SEQ ID:37475, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41626] Another function of VGAM1155 is therefore inhibition of LOC130535 (Accession XM_072244). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC130535. LOC221395 (Accession XM_166354) is another VGAM1155 host target gene. LOC221395 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221395 BINDING SITE, designated SEQ ID:44185, to the nucleotide sequence of VGAM1155 RNA, herein designated VGAM RNA, also designated SEQ ID:3866.

[41627] Another function of VGAM1155 is therefore inhibition of LOC221395 (Accession XM_166354). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221395. LOC91947 (Accession XM_041721) is another VGAM1155 host target gene. LOC91947 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91947, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91947 BINDING SITE, designated SEQ ID:33569, to the nucleotide sequence of VGAM1155 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3866.

[41628] Another function of VGAM1155 is therefore inhibition of LOC91947 (Accession XM_041721). Accordingly, utilities of VGAM1155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91947. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1156 (VGAM1156) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41629] VGAM1156 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1156 was detected is described hereinabove with reference to Figs. 1–8.

[41630] VGAM1156 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41631] VGAM1156 gene encodes a VGAM1156 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1156 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1156 precursor RNA is designated SEQ ID:1142, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1142 is located at position 134779 relative to the genome of Camelpox Virus.

[41632] VGAM1156 precursor RNA folds onto itself, forming VGAM1156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41633] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1156 folded precursor RNA into VGAM1156 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1156 RNA is designated SEQ ID:3867, and is provided hereinbelow with reference to the sequence listing part.

[41634] VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1156 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41635] VGAM1156 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1156 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1156 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41636] The complementary binding of VGAM1156 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1156 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1156 host target RNA into VGAM1156 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41637] It is appreciated that VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1156 host target genes. The mRNA of

each one of this plurality of VGAM1156 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1156 RNA, herein designated VGAM RNA, and which when bound by VGAM1156 RNA causes inhibition of translation of respective one or more VGAM1156 host target proteins.

[41638] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1156 gene, herein designated VGAM GENE, on one or more VGAM1156 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[41639] It is yet further appreciated that a function of VGAM1156 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1156 correlate with, and may be deduced from, the identity of the host target genes which VGAM1156 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41640] Nucleotide sequences of the VGAM1156 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1156 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1156 are further described hereinbelow with reference to Table 1.

[41641] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1156 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1156 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41642] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1156 gene, herein designated VGAM is inhibition of expression of VGAM1156 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1156 correlate with, and may be deduced from, the identity of the target genes which VGAM1156 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41643] BDG-29 (Accession XM_051343) is a VGAM1156 host target gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35816, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41644] A function of VGAM1156 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BDG-29. Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940) is another VGAM1156 host target gene. C21orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf6 BINDING SITE, designated SEQ ID:18855, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41645] Another function of VGAM1156 is therefore inhibition of Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf6. DKFZp434D177 (Accession NM_032264) is another VGAM1156 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:26007, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41646] Another function of VGAM1156 is therefore inhibition of DKFZp434D177 (Accession NM_032264). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434D177. HSA249128 (Accession NM_017583) is another VGAM1156 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19027, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41647] Another function of VGAM1156 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with HSA249128. KIAA1634 (Accession XM_032749) is another VGAM1156 host target gene. KIAA1634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1634 BINDING SITE, designated SEQ ID:31751, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41648] Another function of VGAM1156 is therefore inhibition of KIAA1634 (Accession XM_032749). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1634. KIAA1941 (Accession XM_059318) is another VGAM1156 host target gene. KIAA1941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1941 BINDING SITE, designated SEQ ID:36951, to the

nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41649] Another function of VGAM1156 is therefore inhibition of KIAA1941 (Accession XM_059318). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1941. PRO2533 (Accession NM_018629) is another VGAM1156 host target gene. PRO2533 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2533 BINDING SITE, designated SEQ ID:20702, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41650] Another function of VGAM1156 is therefore inhibition of PRO2533 (Accession NM_018629). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2533. LOC151201 (Accession XM_098021) is another VGAM1156 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41323, to the nucleotide sequence of VGAM1156 RNA, herein designated VGAM RNA, also designated SEQ ID:3867.

[41651] Another function of VGAM1156 is therefore inhibition of LOC151201 (Accession XM_098021). Accordingly, utilities of VGAM1156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1157 (VGAM1157) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41652] VGAM1157 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1157 was detected is described hereinabove with reference to Figs. 1-8.

[41653] VGAM1157 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Camelpox Virus.

VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41654] VGAM1157 gene encodes a VGAM1157 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1157 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1157 precursor RNA is designated SEQ ID:1143, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1143 is located at position 135685 relative to the genome of Camelpox Virus.

[41655] VGAM1157 precursor RNA folds onto itself, forming VGAM1157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41656] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1157 folded precursor RNA into VGAM1157 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1157 RNA is designated SEQ ID:3868, and is provided hereinbelow with reference to the sequence listing part.

[41657] VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1157 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41658] VGAM1157 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1157 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1157 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41659] The complementary binding of VGAM1157 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1157 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1157

host target RNA into VGAM1157 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41660] It is appreciated that VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1157 host target genes. The mRNA of each one of this plurality of VGAM1157 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1157 RNA, herein designated VGAM RNA, and which when bound by VGAM1157 RNA causes inhibition of translation of respective one or more VGAM1157 host target proteins.

[41661] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1157 gene, herein designated VGAM GENE, on one or more VGAM1157 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41662] It is yet further appreciated that a function of VGAM1157 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1157 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1157 correlate with, and may be deduced from, the identity of the host target genes which VGAM1157 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41663] Nucleotide sequences of the VGAM1157 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1157 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1157 are further

described hereinbelow with reference to Table 1.

[41664] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1157 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1157 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41665] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1157 gene, herein designated VGAM is inhibition of expression of VGAM1157 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1157 correlate with, and may be deduced from, the identity of the target genes which VGAM1157 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41666] Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180) is a VGAM1157 host target gene. NTRK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTRK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of NTRK2 BINDING SITE, designated SEQ ID:12841, to the nucleotide sequence of VGAM1157 RNA, herein designated VGAM RNA, also designated SEQ ID:3868.

[41667] A function of VGAM1157 is therefore inhibition of Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180), a gene which is involved in the development and/or maintenance of the nervous system. Accordingly, utilities of VGAM1157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTRK2. The function of NTRK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341.LOC116143 (Accession XM_057465) is another VGAM1157 host target gene. LOC116143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116143 BINDING SITE, designated SEQ ID:36516, to the nucleotide sequence of VGAM1157 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3868.

[41668] Another function of VGAM1157 is therefore inhibition of LOC116143 (Accession XM_057465). Accordingly, utilities of VGAM1157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116143. LOC151121 (Accession XM_087102) is another VGAM1157 host target gene. LOC151121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151121 BINDING SITE, designated SEQ ID:39050, to the nucleotide sequence of VGAM1157 RNA, herein designated VGAM RNA, also designated SEQ ID:3868.

[41669] Another function of VGAM1157 is therefore inhibition of LOC151121 (Accession XM_087102). Accordingly, utilities of VGAM1157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151121. LOC203429 (Accession XM_114701) is another VGAM1157 host target gene. LOC203429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203429, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203429 BINDING SITE, designated SEQ ID:43046, to the nucleotide sequence of VGAM1157 RNA, herein designated VGAM RNA, also designated SEQ ID:3868.

[41670] Another function of VGAM1157 is therefore inhibition of LOC203429 (Accession XM_114701). Accordingly, utilities of VGAM1157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203429. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1158 (VGAM1158) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41671] VGAM1158 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1158 was detected is described hereinabove with reference to Figs. 1-8.

[41672] VGAM1158 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox Virus.

VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41673] VGAM1158 gene encodes a VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1158 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1158 precursor RNA is designated SEQ ID:1144, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1144 is located at position 104200 relative to the genome of Swinepox Virus.

[41674] VGAM1158 precursor RNA folds onto itself, forming VGAM1158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41675] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1158 folded precursor RNA into VGAM1158 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1158 RNA is designated SEQ ID:3869, and is provided hereinbelow with reference to the sequence listing part.

[41676] VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1158 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41677] VGAM1158 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1158 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1158 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41678] The complementary binding of VGAM1158 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1158 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1158 host target RNA into VGAM1158 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41679] It is appreciated that VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1158 host target genes. The mRNA of each one of this plurality of VGAM1158 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1158 RNA, herein designated VGAM RNA, and which when bound by VGAM1158 RNA causes inhibition of translation of respective one or more VGAM1158 host target proteins.

[41680] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1158 gene, herein designated VGAM GENE, on one or more VGAM1158 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41681] It is yet further appreciated that a function of VGAM1158 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of viral infection by Swinepox Virus. Specific functions, and accordingly utilities, of VGAM1158 correlate with, and may be deduced from, the identity of the host target genes which VGAM1158 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41682] Nucleotide sequences of the VGAM1158 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1158 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1158 are further described hereinbelow with reference to Table 1.

[41683] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1158 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1158 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41684] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1158 gene, herein designated VGAM is inhibition of expression of VGAM1158 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1158 correlate with, and may be deduced from, the identity of the target genes which VGAM1158 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41685] AS3 (Accession NM_015928) is a VGAM1158 host target gene. AS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AS3 BINDING SITE, designated SEQ ID:18051, to the nucleotide sequence of VGAM1158 RNA, herein

designated VGAM RNA, also designated SEQ ID:3869.

[41686] A function of VGAM1158 is therefore inhibition of AS3 (Accession NM_015928), a gene which inhibits cell proliferation. Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AS3. The function of AS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM393.Mannosidase, Alpha, Class 1A, Member 1 (MAN1A1, Accession XM_166312) is another VGAM1158 host target gene. MAN1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1A1 BINDING SITE, designated SEQ ID:44136, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41687] Another function of VGAM1158 is therefore inhibition of Mannosidase, Alpha, Class 1A, Member 1 (MAN1A1, Accession XM_166312), a gene which removes 3 distinct

mannose residues from peptide-bound Man(9)–GlcNAc(2) oligosaccharides. Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1A1. The function of MAN1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM_000620) is another VGAM1158 host target gene. NOS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NOS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOS1 BINDING SITE, designated SEQ ID:6234, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41688] Another function of VGAM1158 is therefore inhibition of Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM_000620), a gene which produces nitric oxide (no) which is a messenger molecule with diverse functions throughout the body. Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with NOS1. The function of NOS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM323.UDP-GlcNAc:betaGal Beta-

1,3-N-acetylglucosaminyltransferase 1 (B3GNT1, Accession NM_006577) is another VGAM1158 host target gene.

B3GNT1 BINDING SITE1 and B3GNT1 BINDING SITE2 are

HOST TARGET binding sites found in untranslated regions

of mRNA encoded by B3GNT1, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING

SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of B3GNT1 BINDING

SITE1 and B3GNT1 BINDING SITE2, designated SEQ

ID:13344 and SEQ ID:27087 respectively, to the nu-

cleotide sequence of VGAM1158 RNA, herein designated

VGAM RNA, also designated SEQ ID:3869.

[41689] Another function of VGAM1158 is therefore inhibition of UDP-GlcNAc:betaGal Beta-

1,3-N-acetylglucosaminyltransferase 1 (B3GNT1, Accession NM_006577). Accordingly, utilities of VGAM1158 in-

clude diagnosis, prevention and treatment of diseases and

clinical conditions associated with B3GNT1. GTPBG3

(Accession NM_032620) is another VGAM1158 host target gene. GTPBG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTPBG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTPBG3 BINDING SITE, designated SEQ ID:26336, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41690] Another function of VGAM1158 is therefore inhibition of GTPBG3 (Accession NM_032620). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTPBG3. KIAA0792 (Accession NM_014698) is another VGAM1158 host target gene. KIAA0792 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0792, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0792 BINDING SITE, designated SEQ ID:16213, to the nucleotide sequence of VGAM1158 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3869.

[41691] Another function of VGAM1158 is therefore inhibition of KIAA0792 (Accession NM_014698). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0792. KIAA0979 (Accession NM_015032) is another VGAM1158 host target gene. KIAA0979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0979 BINDING SITE, designated SEQ ID:17389, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41692] Another function of VGAM1158 is therefore inhibition of KIAA0979 (Accession NM_015032). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0979. KIAA0981 (Accession XM_028867) is another VGAM1158 host target gene. KIAA0981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0981, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0981 BINDING SITE, designated SEQ ID:30796, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41693] Another function of VGAM1158 is therefore inhibition of KIAA0981 (Accession XM_028867). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0981. KIAA1462 (Accession XM_166132) is another VGAM1158 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43919, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41694] Another function of VGAM1158 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1462. ZAK (Accession NM_016653) is another VGAM1158 host target gene. ZAK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZAK BINDING SITE, designated SEQ ID:18779, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41695] Another function of VGAM1158 is therefore inhibition of ZAK (Accession NM_016653). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZAK. LOC138515 (Accession XM_070943) is another VGAM1158 host target gene. LOC138515 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138515 BINDING SITE, designated SEQ ID:37395, to

the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41696] Another function of VGAM1158 is therefore inhibition of LOC138515 (Accession XM_070943). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138515. LOC254249 (Accession XM_170931) is another VGAM1158 host target gene. LOC254249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254249 BINDING SITE, designated SEQ ID:45713, to the nucleotide sequence of VGAM1158 RNA, herein designated VGAM RNA, also designated SEQ ID:3869.

[41697] Another function of VGAM1158 is therefore inhibition of LOC254249 (Accession XM_170931). Accordingly, utilities of VGAM1158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1159 (VGAM1159) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41698] VGAM1159 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1159 was detected is described hereinabove with reference to Figs. 1–8.

[41699] VGAM1159 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41700] VGAM1159 gene encodes a VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1159 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1159 precursor RNA is designated SEQ ID:1145, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1145 is located at position 38413 relative to the genome of Meleagrid Herpesvirus 1.

[41701] VGAM1159 precursor RNA folds onto itself, forming VGAM1159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41702] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1159 folded precursor RNA into VGAM1159 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1159 RNA is designated SEQ ID:3870, and is provided hereinbelow with reference to the sequence listing part.

[41703] VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1159 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1159 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41704] VGAM1159 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1159 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1159 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41705] The complementary binding of VGAM1159 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1159 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1159 host target RNA into VGAM1159 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41706] It is appreciated that VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1159 host target genes. The mRNA of each one of this plurality of VGAM1159 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1159 RNA, herein designated VGAM RNA, and which when bound by VGAM1159 RNA causes inhibition of translation of respective one or more VGAM1159 host target proteins.

[41707] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1159 gene, herein designated VGAM GENE, on one or more VGAM1159 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41708] It is yet further appreciated that a function of VGAM1159 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1159 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1159 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41709] Nucleotide sequences of the VGAM1159 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1159 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1159 are further described hereinbelow with reference to Table 1.

[41710] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1159 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1159 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41711] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1159 gene, herein designated VGAM is inhibition of expression of VGAM1159 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1159 correlate with, and may be deduced from, the identity of the target genes which VGAM1159

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41712] Complement Component 7 (C7, Accession NM_000587) is a VGAM1159 host target gene. C7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7 BINDING SITE, designated SEQ ID:6191, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41713] A function of VGAM1159 is therefore inhibition of Complement Component 7 (C7, Accession NM_000587). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7. FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801) is another VGAM1159 host target gene. FKBP1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FKBP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FKBP1A BINDING SITE, designated SEQ ID:6475, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41714] Another function of VGAM1159 is therefore inhibition of FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801), a gene which FK506-binding protein 1A. Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP1A. The function of FKBP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is another VGAM1159 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28941, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3870.

[41715] Another function of VGAM1159 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. FENS-1 (Accession NM_020830) is another VGAM1159 host target gene. FENS-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FENS-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FENS-1 BINDING SITE, designated SEQ ID:21896, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41716] Another function of VGAM1159 is therefore inhibition of FENS-1 (Accession NM_020830). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FENS-1. FLJ12592 (Accession NM_032169) is another VGAM1159 host target gene. FLJ12592 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ12592, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12592 BINDING SITE, designated SEQ ID:25874, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41717] Another function of VGAM1159 is therefore inhibition of FLJ12592 (Accession NM_032169). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12592. FLJ20079 (Accession NM_017656) is another VGAM1159 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19179, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41718] Another function of VGAM1159 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of

VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. KIAA0143 (Accession XM_035825) is another VGAM1159 host target gene. KIAA0143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0143 BINDING SITE, designated SEQ ID:32352, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41719] Another function of VGAM1159 is therefore inhibition of KIAA0143 (Accession XM_035825). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0143. KIAA0420 (Accession XM_032693) is another VGAM1159 host target gene. KIAA0420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0420 BINDING SITE, designated SEQ ID:31726, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41720] Another function of VGAM1159 is therefore inhibition of KIAA0420 (Accession XM_032693). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0420. PRO2266 (Accession NM_018519) is another VGAM1159 host target gene. PRO2266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2266 BINDING SITE, designated SEQ ID:20597, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41721] Another function of VGAM1159 is therefore inhibition of PRO2266 (Accession NM_018519). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2266. SCYD1 (Accession XM_165650) is another VGAM1159 host target gene. SCYD1 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by SCYD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYD1 BINDING SITE, designated SEQ ID:43713, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41722] Another function of VGAM1159 is therefore inhibition of SCYD1 (Accession XM_165650). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYD1. LOC115265 (Accession XM_055596) is another VGAM1159 host target gene. LOC115265 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115265 BINDING SITE, designated SEQ ID:36310, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41723] Another function of VGAM1159 is therefore inhibition of

LOC115265 (Accession XM_055596). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115265. LOC164375 (Accession XM_104379) is another VGAM1159 host target gene. LOC164375 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164375, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164375 BINDING SITE, designated SEQ ID:42158, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41724] Another function of VGAM1159 is therefore inhibition of LOC164375 (Accession XM_104379). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164375. LOC253776 (Accession XM_173240) is another VGAM1159 host target gene. LOC253776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC253776 BINDING SITE, designated SEQ ID:46526, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41725] Another function of VGAM1159 is therefore inhibition of LOC253776 (Accession XM_173240). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253776. LOC255696 (Accession XM_173933) is another VGAM1159 host target gene. LOC255696 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255696 BINDING SITE, designated SEQ ID:46568, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41726] Another function of VGAM1159 is therefore inhibition of LOC255696 (Accession XM_173933). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255696. LOC257354 (Accession XM_170810) is an-

other VGAM1159 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45579, to the nucleotide sequence of VGAM1159 RNA, herein designated VGAM RNA, also designated SEQ ID:3870.

[41727] Another function of VGAM1159 is therefore inhibition of LOC257354 (Accession XM_170810). Accordingly, utilities of VGAM1159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1160 (VGAM1160) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41728] VGAM1160 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1160 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[41729] VGAM1160 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41730] VGAM1160 gene encodes a VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1160 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1160 precursor RNA is designated SEQ ID:1146, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1146 is located at position 39108 relative to the genome of Meleagrid Herpesvirus 1.

[41731] VGAM1160 precursor RNA folds onto itself, forming VGAM1160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41732] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1160 folded precursor RNA into VGAM1160 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM1160 RNA is designated SEQ ID:3871, and is provided hereinbelow with reference to the sequence listing part.

[41733] VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1160 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41734] VGAM1160 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1160 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1160 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1160 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41735] The complementary binding of VGAM1160 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1160 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1160 host target RNA into VGAM1160 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41736] It is appreciated that VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1160 host target genes. The mRNA of each one of this plurality of VGAM1160 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1160 RNA, herein designated VGAM RNA, and which when bound by VGAM1160 RNA causes inhibition of translation of respective one or more VGAM1160 host target proteins.

[41737] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1160 gene, herein designated VGAM GENE, on one or more VGAM1160 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41738] It is yet further appreciated that a function of VGAM1160 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1160 correlate with, and may be deduced from, the identity of the host target genes which VGAM1160 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41739] Nucleotide sequences of the VGAM1160 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1160 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1160 are further described hereinbelow with reference to Table 1.

[41740] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1160 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1160 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41741] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1160 gene, herein designated VGAM is inhibition of expression of VGAM1160 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1160 correlate with, and may be deduced from, the identity of the target genes which VGAM1160 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41742] Basic Transcription Element Binding Protein 1 (BTEB1, Accession NM_001206) is a VGAM1160 host target gene. BTEB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BTEB1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTEB1 BINDING SITE, designated SEQ ID:6870, to the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, also designated SEQ ID:3871.

[41743] A function of VGAM1160 is therefore inhibition of Basic Transcription Element Binding Protein 1 (BTEB1, Accession NM_001206). Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTEB1. DKFZP434I1735 (Accession XM_113763) is another VGAM1160 host target gene. DKFZP434I1735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434I1735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I1735 BINDING SITE, designated SEQ ID:42420, to the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, also designated SEQ ID:3871.

[41744] Another function of VGAM1160 is therefore inhibition of DKFZP434I1735 (Accession XM_113763). Accordingly, utilities of VGAM1160 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434I1735. FLJ23598 (Accession NM_024783) is another VGAM1160 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24154, to the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, also designated SEQ ID:3871.

[41745] Another function of VGAM1160 is therefore inhibition of FLJ23598 (Accession NM_024783). Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. LOC149711 (Accession XM_097720) is another VGAM1160 host target gene. LOC149711 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149711 BINDING SITE, designated SEQ ID:41074, to

the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, also designated SEQ ID:3871.

[41746] Another function of VGAM1160 is therefore inhibition of LOC149711 (Accession XM_097720). Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149711. LOC199988 (Accession XM_117166) is another VGAM1160 host target gene. LOC199988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199988 BINDING SITE, designated SEQ ID:43268, to the nucleotide sequence of VGAM1160 RNA, herein designated VGAM RNA, also designated SEQ ID:3871.

[41747] Another function of VGAM1160 is therefore inhibition of LOC199988 (Accession XM_117166). Accordingly, utilities of VGAM1160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199988. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1161 (VGAM1161) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41748] VGAM1161 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1161 was detected is described hereinabove with reference to Figs. 1–8.

[41749] VGAM1161 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Meleagrid Herpesvirus 1. VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41750] VGAM1161 gene encodes a VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1161 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1161 precursor RNA is designated SEQ ID:1147, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1147 is located at position 38258 relative to the genome of Meleagrid Herpesvirus 1.

[41751] VGAM1161 precursor RNA folds onto itself, forming VGAM1161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41752] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1161 folded precursor RNA into VGAM1161 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1161 RNA is designated SEQ ID:3872, and is provided hereinbelow with reference to the sequence listing part.

[41753] VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1161 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1161 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[41754] VGAM1161 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1161 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1161 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41755] The complementary binding of VGAM1161 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1161 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1161 host target RNA into VGAM1161 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41756] It is appreciated that VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1161 host target genes. The mRNA of each one of this plurality of VGAM1161 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1161 RNA, herein designated VGAM RNA, and which when bound by VGAM1161 RNA causes inhibition of translation of respective one or more VGAM1161 host target proteins.

[41757] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1161 gene, herein designated VGAM GENE, on one or more VGAM1161 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41758] It is yet further appreciated that a function of VGAM1161 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1161 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1161 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41759] Nucleotide sequences of the VGAM1161 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1161 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1161 are further described hereinbelow with reference to Table 1.

[41760] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1161 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1161 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41761] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1161 gene, herein designated VGAM is inhibition of expression of VGAM1161 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1161 correlate with, and may be deduced from, the identity of the target genes which VGAM1161

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41762] LOC203276 (Accession XM_117523) is a VGAM1161 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43486, to the nucleotide sequence of VGAM1161 RNA, herein designated VGAM RNA, also designated SEQ ID:3872.

[41763] A function of VGAM1161 is therefore inhibition of LOC203276 (Accession XM_117523). Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM_117529) is another VGAM1161 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC203305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC203305 BINDING SITE, designated SEQ ID:43510, to the nucleotide sequence of VGAM1161 RNA, herein designated VGAM RNA, also designated SEQ ID:3872.

[41764] Another function of VGAM1161 is therefore inhibition of LOC203305 (Accession XM_117529). Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC254243 (Accession XM_173233) is another VGAM1161 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46512, to the nucleotide sequence of VGAM1161 RNA, herein designated VGAM RNA, also designated SEQ ID:3872.

[41765] Another function of VGAM1161 is therefore inhibition of LOC254243 (Accession XM_173233). Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC90038 (Accession XM_028305) is another VGAM1161 host target gene. LOC90038 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30649, to the nucleotide sequence of VGAM1161 RNA, herein designated VGAM RNA, also designated SEQ ID:3872.

[41766] Another function of VGAM1161 is therefore inhibition of LOC90038 (Accession XM_028305). Accordingly, utilities of VGAM1161 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1162 (VGAM1162) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41767] VGAM1162 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1162 was detected is described hereinabove with reference to Figs. 1-8.

[41768] VGAM1162 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41769] VGAM1162 gene encodes a VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1162 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1162 precursor RNA is designated SEQ ID:1148, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1148 is located at position 139277 relative to the genome of Ectromelia Virus.

[41770] VGAM1162 precursor RNA folds onto itself, forming VGAM1162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[41771] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1162 folded precursor RNA into VGAM1162 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1162 RNA is designated SEQ ID:3873, and is provided hereinbelow with reference to the sequence listing part.

[41772] VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1162 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41773] VGAM1162 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1162 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1162 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1162 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41774] The complementary binding of VGAM1162 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1162 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1162 host target RNA into VGAM1162 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41775] It is appreciated that VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1162 host target genes. The mRNA of each one of this plurality of VGAM1162 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1162 RNA, herein designated VGAM RNA, and which when bound by VGAM1162 RNA causes inhibition of translation of respective one or more VGAM1162 host target proteins.

[41776] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1162 gene, herein designated VGAM GENE, on one or more VGAM1162 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41777] It is yet further appreciated that a function of VGAM1162 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1162 correlate with, and may be deduced from, the identity of the host target genes which VGAM1162 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41778] Nucleotide sequences of the VGAM1162 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1162 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1162 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1162 are further described hereinbelow with reference to Table 1.

[41779] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1162 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1162 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41780] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1162 gene, herein designated VGAM is inhibition of expression of VGAM1162 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1162 correlate with, and may be deduced from, the identity of the target genes which VGAM1162 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41781] Bullous Pemphigoid Antigen 1, 230/240kDa (BPAG1, Accession NM_015548) is a VGAM1162 host target gene. BPAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BPAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of BPAG1 BINDING SITE, designated SEQ ID:17811, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41782] A function of VGAM1162 is therefore inhibition of Bullous Pemphigoid Antigen 1, 230/240kDa (BPAG1, Accession NM_015548), a gene which plays a role in cross-linking actin to other cytoskeletal proteins, binds to microtubules. Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BPAG1. The function of BPAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM494.CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838) is another VGAM1162 host target gene. CSMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE, designated SEQ ID:36189, to the

nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41783] Another function of VGAM1162 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. KIAA1987 (Accession XM_113870) is another VGAM1162 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42501, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41784] Another function of VGAM1162 is therefore inhibition of KIAA1987 (Accession XM_113870). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. Leucine-rich Repeat LGI Family, Member 2 (LGI2, Accession NM_018176) is another VGAM1162 host

target gene. LGI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LGI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGI2 BINDING SITE, designated SEQ ID:20002, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41785] Another function of VGAM1162 is therefore inhibition of Leucine-rich Repeat LGI Family, Member 2 (LGI2, Accession NM_018176). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGI2. VEST1 (Accession NM_052958) is another VGAM1162 host target gene. VEST1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VEST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VEST1 BINDING SITE, designated SEQ ID:27519, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ

ID:3873.

[41786] Another function of VGAM1162 is therefore inhibition of VEST1 (Accession NM_052958). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEST1. LOC145945 (Accession XM_096908) is another VGAM1162 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40638, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41787] Another function of VGAM1162 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC149013 (Accession XM_086398) is another VGAM1162 host target gene. LOC149013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149013, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149013 BINDING SITE, designated SEQ ID:38632, to the nucleotide sequence of VGAM1162 RNA, herein designated VGAM RNA, also designated SEQ ID:3873.

[41788] Another function of VGAM1162 is therefore inhibition of LOC149013 (Accession XM_086398). Accordingly, utilities of VGAM1162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149013. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1163 (VGAM1163) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41789] VGAM1163 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1163 was detected is described hereinabove with reference to Figs. 1-8.

[41790] VGAM1163 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ectromelia Virus.

VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41791] VGAM1163 gene encodes a VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1163 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1163 precursor RNA is designated SEQ ID:1149, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1149 is located at position 140623 relative to the genome of Ectromelia Virus.

[41792] VGAM1163 precursor RNA folds onto itself, forming VGAM1163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41793] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1163 folded precursor RNA into VGAM1163 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM1163 RNA is designated SEQ ID:3874, and is provided hereinbelow with reference to the sequence listing part.

[41794] VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1163 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41795] VGAM1163 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1163 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1163 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41796] The complementary binding of VGAM1163 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1163 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1163 host target RNA into VGAM1163 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41797] It is appreciated that VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1163 host target genes. The mRNA of each one of this plurality of VGAM1163 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1163 RNA, herein designated VGAM RNA, and which when bound by VGAM1163 RNA causes inhibition of translation of respective one or more VGAM1163 host target proteins.

[41798] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1163 gene, herein designated VGAM GENE, on one or more VGAM1163 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41799] It is yet further appreciated that a function of VGAM1163 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1163 correlate with, and may be deduced from, the identity of the host target genes which VGAM1163 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41800] Nucleotide sequences of the VGAM1163 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1163 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1163 are further described hereinbelow with reference to Table 1.

[41801] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1163 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1163 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41802] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1163 gene, herein designated VGAM is inhibition of expression of VGAM1163 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1163 correlate with, and may be deduced from, the identity of the target genes which VGAM1163 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41803] ATPase, Class V, Type 10B (ATP10B, Accession XM_032721) is a VGAM1163 host target gene. ATP10B BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by ATP10B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10B BINDING SITE, designated SEQ ID:31735, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41804] A function of VGAM1163 is therefore inhibition of ATPase, Class V, Type 10B (ATP10B, Accession XM_032721). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10B. BDG-29 (Accession XM_051343) is another VGAM1163 host target gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35815, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41805] Another function of VGAM1163 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of

VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BDG-29. GW112 (Accession NM_006418) is another VGAM1163 host target gene. GW112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GW112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GW112 BINDING SITE, designated SEQ ID:13131, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41806] Another function of VGAM1163 is therefore inhibition of GW112 (Accession NM_006418). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GW112. Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424) is another VGAM1163 host target gene. HSPB7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of HSPB7 BINDING SITE, designated SEQ ID:15780, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41807] Another function of VGAM1163 is therefore inhibition of Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPB7. KIAA1464 (Accession XM_043069) is another VGAM1163 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33882, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41808] Another function of VGAM1163 is therefore inhibition of KIAA1464 (Accession XM_043069). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1464. KIAA1634 (Accession XM_032749) is another VGAM1163 host target gene. KIAA1634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1634 BINDING SITE, designated SEQ ID:31752, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41809] Another function of VGAM1163 is therefore inhibition of KIAA1634 (Accession XM_032749). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1634. Neuropilin (NRP) and Tolloid (TLL)-like 1 (NETO1, Accession NM_138999) is another VGAM1163 host target gene. NETO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NETO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NETO1 BINDING SITE, designated SEQ ID:29097, to the nucleotide sequence of

VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41810] Another function of VGAM1163 is therefore inhibition of Neuropilin (NRP) and Tolloid (TLL)-like 1 (NETO1, Accession NM_138999). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NETO1. PRO2533 (Accession NM_018629) is another VGAM1163 host target gene. PRO2533 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2533 BINDING SITE, designated SEQ ID:20703, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41811] Another function of VGAM1163 is therefore inhibition of PRO2533 (Accession NM_018629). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2533. LOC151201 (Accession XM_098021) is another VGAM1163 host target gene. LOC151201 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41324, to the nucleotide sequence of VGAM1163 RNA, herein designated VGAM RNA, also designated SEQ ID:3874.

[41812] Another function of VGAM1163 is therefore inhibition of LOC151201 (Accession XM_098021). Accordingly, utilities of VGAM1163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1164 (VGAM1164) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41813] VGAM1164 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1164 was detected is described hereinabove with reference to Figs. 1-8.

[41814] VGAM1164 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41815] VGAM1164 gene encodes a VGAM1164 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1164 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1164 precursor RNA is designated SEQ ID:1150, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1150 is located at position 135687 relative to the genome of Camelpox Virus.

[41816] VGAM1164 precursor RNA folds onto itself, forming VGAM1164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[41817] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1164 folded precursor RNA into VGAM1164 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1164 RNA is designated SEQ ID:3875, and is provided hereinbelow with reference to the sequence listing part.

[41818] VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1164 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41819] VGAM1164 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1164 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1164 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1164 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[41820] The complementary binding of VGAM1164 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1164 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1164 host target RNA into VGAM1164 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41821] It is appreciated that VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1164 host target genes. The mRNA of each one of this plurality of VGAM1164 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1164 RNA, herein designated VGAM RNA, and which when bound by VGAM1164 RNA causes inhibition of translation of respective one or more VGAM1164 host target proteins.

[41822] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1164 gene, herein designated VGAM GENE, on one or more VGAM1164 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41823] It is yet further appreciated that a function of VGAM1164 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1164 correlate with, and may be deduced from, the identity of the host target genes which VGAM1164 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41824] Nucleotide sequences of the VGAM1164 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1164 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1164 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1164 are further described hereinbelow with reference to Table 1.

[41825] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1164 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1164 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41826] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1164 gene, herein designated VGAM is inhibition of expression of VGAM1164 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1164 correlate with, and may be deduced from, the identity of the target genes which VGAM1164 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41827] Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180) is a VGAM1164 host target gene. NTRK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTRK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of NTRK2 BINDING SITE, designated SEQ ID:12841, to the nucleotide sequence of VGAM1164 RNA, herein designated VGAM RNA, also designated SEQ ID:3875.

[41828] A function of VGAM1164 is therefore inhibition of Neurotrophic Tyrosine Kinase, Receptor, Type 2 (NTRK2, Accession NM_006180), a gene which is involved in the development and/or maintenance of the nervous system. Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTRK2. The function of NTRK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM341. LOC116143 (Accession XM_057465) is another VGAM1164 host target gene. LOC116143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116143 BINDING SITE, designated SEQ ID:36516, to

the nucleotide sequence of VGAM1164 RNA, herein designated VGAM RNA, also designated SEQ ID:3875.

[41829] Another function of VGAM1164 is therefore inhibition of LOC116143 (Accession XM_057465). Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116143. LOC151121 (Accession XM_087102) is another VGAM1164 host target gene. LOC151121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151121 BINDING SITE, designated SEQ ID:39050, to the nucleotide sequence of VGAM1164 RNA, herein designated VGAM RNA, also designated SEQ ID:3875.

[41830] Another function of VGAM1164 is therefore inhibition of LOC151121 (Accession XM_087102). Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151121. LOC203429 (Accession XM_114701) is another VGAM1164 host target gene. LOC203429 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC203429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203429 BINDING SITE, designated SEQ ID:43046, to the nucleotide sequence of VGAM1164 RNA, herein designated VGAM RNA, also designated SEQ ID:3875.

[41831] Another function of VGAM1164 is therefore inhibition of LOC203429 (Accession XM_114701). Accordingly, utilities of VGAM1164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203429. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1165 (VGAM1165) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41832] VGAM1165 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1165 was detected is described hereinabove with reference to Figs. 1-8.

[41833] VGAM1165 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Ectromelia Virus.

VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41834] VGAM1165 gene encodes a VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1165 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1165 precursor RNA is designated SEQ ID:1151, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1151 is located at position 141338 relative to the genome of Ectromelia Virus.

[41835] VGAM1165 precursor RNA folds onto itself, forming VGAM1165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41836] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1165 folded precursor RNA into VGAM1165 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1165 RNA is designated SEQ ID:3876, and is provided hereinbelow with reference to the sequence listing part.

[41837] VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1165 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41838] VGAM1165 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1165 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1165 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41839] The complementary binding of VGAM1165 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1165 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1165

host target RNA into VGAM1165 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41840] It is appreciated that VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1165 host target genes. The mRNA of each one of this plurality of VGAM1165 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1165 RNA, herein designated VGAM RNA, and which when bound by VGAM1165 RNA causes inhibition of translation of respective one or more VGAM1165 host target proteins.

[41841] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1165 gene, herein designated VGAM GENE, on one or more VGAM1165 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41842] It is yet further appreciated that a function of VGAM1165 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGAM1165 correlate with, and may be deduced from, the identity of the host target genes which VGAM1165 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41843] Nucleotide sequences of the VGAM1165 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1165 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1165 are further

described hereinbelow with reference to Table 1.

[41844] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1165 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1165 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41845] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1165 gene, herein designated VGAM is inhibition of expression of VGAM1165 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1165 correlate with, and may be deduced from, the identity of the target genes which VGAM1165 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41846] Apolipoprotein B mRNA Editing Enzyme, Catalytic Polypeptide 1 (APOBEC1, Accession NM_005889) is a VGAM1165 host target gene. APOBEC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOBEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of APOBEC1 BINDING SITE, designated SEQ ID:12508, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41847] A function of VGAM1165 is therefore inhibition of Apolipoprotein B mRNA Editing Enzyme, Catalytic Polypeptide 1 (APOBEC1, Accession NM_005889). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOBEC1. Bridging Integrator 3 (BIN3, Accession NM_018688) is another VGAM1165 host target gene. BIN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BIN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIN3 BINDING SITE, designated SEQ ID:20762, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41848] Another function of VGAM1165 is therefore inhibition of Bridging Integrator 3 (BIN3, Accession NM_018688). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with BIN3. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397) is another VGAM1165 host target gene. DDX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX6 BINDING SITE, designated SEQ ID:10642, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41849] Another function of VGAM1165 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397), a gene which is putative RNA helicases. Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX6. The function of DDX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179.Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM_000132) is another VGAM1165 host target gene. F8 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by F8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F8 BINDING SITE, designated SEQ ID:5617, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41850] Another function of VGAM1165 is therefore inhibition of Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM_000132). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F8. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is another VGAM1165 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7735, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41851] Another function of VGAM1165 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Alpha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944) is another VGAM1165 host target gene. PPP3CA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP3CA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP3CA BINDING SITE, designated SEQ ID:6645, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41852] Another function of VGAM1165 is therefore inhibition of Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Al-

pha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944), a gene which is the catalytic subunit of calcium-dependent, calmodulin-stimulated protein phosphatase. Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP3CA. The function of PPP3CA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497.RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732) is another VGAM1165 host target gene. RAD50 BINDING SITE1 and RAD50 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD50, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD50 BINDING SITE1 and RAD50 BINDING SITE2, designated SEQ ID:12297 and SEQ ID:28555 respectively, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41853] Another function of VGAM1165 is therefore inhibition of RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession

NM_005732), a gene which is involved in dna double-strand break repair (dsbr). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD50. The function of RAD50 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132. KIAA0268 (Accession XM_046126) is another VGAM1165 host target gene. KIAA0268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0268 BINDING SITE, designated SEQ ID:34688, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41854] Another function of VGAM1165 is therefore inhibition of KIAA0268 (Accession XM_046126). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0268. MGC22014 (Accession XM_035307) is another VGAM1165 host target gene. MGC22014 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32222, to the nucleotide sequence of VGAM1165 RNA, herein designated VGAM RNA, also designated SEQ ID:3876.

[41855] Another function of VGAM1165 is therefore inhibition of MGC22014 (Accession XM_035307). Accordingly, utilities of VGAM1165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22014. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1166 (VGAM1166) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41856] VGAM1166 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1166 was detected is described hereinabove with reference to Figs. 1-8.

[41857] VGAM1166 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cucumber Green Mottle Mosaic Virus. VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41858] VGAM1166 gene encodes a VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1166 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1166 precursor RNA is designated SEQ ID:1152, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1152 is located at position 2881 relative to the genome of Cucumber Green Mottle Mosaic Virus.

[41859] VGAM1166 precursor RNA folds onto itself, forming VGAM1166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[41860] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1166 folded precursor RNA into VGAM1166 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1166 RNA is designated SEQ ID:3877, and is provided hereinbelow with reference to the sequence listing part.

[41861] VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1166 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41862] VGAM1166 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1166 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1166 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1166 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[41863] The complementary binding of VGAM1166 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1166 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1166 host target RNA into VGAM1166 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41864] It is appreciated that VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1166 host target genes. The mRNA of each one of this plurality of VGAM1166 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1166 RNA, herein designated VGAM RNA, and which when bound by VGAM1166 RNA causes inhibition of translation of respective one or more VGAM1166 host target proteins.

[41865] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1166 gene, herein designated VGAM GENE, on one or more VGAM1166 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41866] It is yet further appreciated that a function of VGAM1166 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of viral infection by Cucumber Green Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1166 correlate with, and may be deduced from, the identity of the host target genes which VGAM1166 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41867] Nucleotide sequences of the VGAM1166 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1166 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1166 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1166 are further described hereinbelow with reference to Table 1.

[41868] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1166 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1166 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41869] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1166 gene, herein designated VGAM is inhibition of expression of VGAM1166 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1166 correlate with, and may be deduced from, the identity of the target genes which VGAM1166 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41870] RAD54B (Accession NM_134434) is a VGAM1166 host target gene. RAD54B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAD54B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of RAD54B BINDING SITE, designated SEQ ID:28675, to the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, also designated SEQ ID:3877.

[41871] A function of VGAM1166 is therefore inhibition of RAD54B (Accession NM_134434), a gene which is involved in dna repair and mitotic recombination. Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD54B. The function of RAD54B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM_005069) is another VGAM1166 host target gene. SIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM2 BINDING SITE, designated SEQ ID:11519, to the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, also designated SEQ ID:3877.

[41872] Another function of VGAM1166 is therefore inhibition of Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM_005069), a gene which may be a master gene of cns development. Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM2. The function of SIM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM369. TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190) is another VGAM1166 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9180, to the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, also designated SEQ ID:3877.

[41873] Another function of VGAM1166 is therefore inhibition of TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of

VGAM1166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAPBP. The function of TAPBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM122.FHR5 (Accession NM_030787) is another VGAM1166 host target gene. FHR5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHR5 BINDING SITE, designated SEQ ID:25084, to the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, also designated SEQ ID:3877.

[41874] Another function of VGAM1166 is therefore inhibition of FHR5 (Accession NM_030787). Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHR5. LOC145739 (Accession XM_085222) is another VGAM1166 host target gene. LOC145739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145739, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145739 BINDING SITE, designated SEQ ID:37963, to the nucleotide sequence of VGAM1166 RNA, herein designated VGAM RNA, also designated SEQ ID:3877.

[41875] Another function of VGAM1166 is therefore inhibition of LOC145739 (Accession XM_085222). Accordingly, utilities of VGAM1166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145739. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1167 (VGAM1167) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41876] VGAM1167 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1167 was detected is described hereinabove with reference to Figs. 1-8.

[41877] VGAM1167 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cucumber Green Mottle

Mosaic Virus. VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41878] VGAM1167 gene encodes a VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1167 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1167 precursor RNA is designated SEQ ID:1153, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1153 is located at position 2385 relative to the genome of Cucumber Green Mottle Mosaic Virus.

[41879] VGAM1167 precursor RNA folds onto itself, forming VGAM1167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41880] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1167 folded precursor RNA into VGAM1167 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1167 RNA is designated SEQ ID:3878, and is provided hereinbelow with reference to the sequence listing part.

[41881] VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1167 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41882] VGAM1167 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1167 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1167 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41883] The complementary binding of VGAM1167 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1167 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1167 host target RNA into VGAM1167 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41884] It is appreciated that VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1167 host target genes. The mRNA of each one of this plurality of VGAM1167 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1167 RNA, herein designated VGAM RNA, and which when bound by VGAM1167 RNA causes inhibition of translation of respective one or more VGAM1167 host target proteins.

[41885] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1167 gene, herein designated VGAM GENE, on one or more VGAM1167 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41886] It is yet further appreciated that a function of VGAM1167 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of viral infection by Cucumber Green Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1167 correlate with, and may be deduced from, the identity of the host target genes which VGAM1167 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41887] Nucleotide sequences of the VGAM1167 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1167 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1167 are further described hereinbelow with reference to Table 1.

[41888] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1167 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1167 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41889] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1167 gene, herein designated VGAM is inhibition of expression of VGAM1167 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1167 correlate with, and may be deduced from, the identity of the target genes which VGAM1167 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41890] Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398) is a VGAM1167 host target gene. DLG5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DLG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG5 BINDING SITE, designated SEQ ID:40337, to the nu-

cleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, also designated SEQ ID:3878.

[41891] A function of VGAM1167 is therefore inhibition of Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398), a gene which may transmit extracellular signals to inhibit cell proliferation. Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG5. The function of DLG5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444.5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870) is another VGAM1167 host target gene. HTR4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR4 BINDING SITE, designated SEQ ID:6539, to the nucleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, also designated SEQ ID:3878.

[41892] Another function of VGAM1167 is therefore inhibition of

5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870), a gene which mediates calcium channel currents. Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR4. The function of HTR4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM65. Growth Hormone Inducible Transmembrane Protein (GHITM, Accession NM_014394) is another VGAM1167 host target gene. GHITM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHITM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GHITM BINDING SITE, designated SEQ ID:15725, to the nucleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, also designated SEQ ID:3878.

[41893] Another function of VGAM1167 is therefore inhibition of Growth Hormone Inducible Transmembrane Protein (GHITM, Accession NM_014394). Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GHITM. Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580) is another VGAM1167 host target gene. MKRN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MKRN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN2 BINDING SITE, designated SEQ ID:35857, to the nucleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, also designated SEQ ID:3878.

[41894] Another function of VGAM1167 is therefore inhibition of Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580). Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN2. Neuropilin (NRP) and Tolloid (TLL)-like 2 (NETO2, Accession NM_018092) is another VGAM1167 host target gene. NETO2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NETO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of NETO2 BINDING SITE, designated SEQ ID:19860, to the nucleotide sequence of VGAM1167 RNA, herein designated VGAM RNA, also designated SEQ ID:3878.

[41895] Another function of VGAM1167 is therefore inhibition of Neuropilin (NRP) and Tolloid (TLL)-like 2 (NETO2, Accession NM_018092). Accordingly, utilities of VGAM1167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NETO2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1168 (VGAM1168) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41896] VGAM1168 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1168 was detected is described hereinabove with reference to Figs. 1-8.

[41897] VGAM1168 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[41898] VGAM1168 gene encodes a VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1168 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1168 precursor RNA is designated SEQ ID:1154, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1154 is located at position 92139 relative to the genome of Rana Tigrina Ranavirus.

[41899] VGAM1168 precursor RNA folds onto itself, forming VGAM1168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41900] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1168 folded precursor RNA into VGAM1168 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1168 RNA is designated SEQ ID:3879, and is provided hereinbelow with reference to the sequence listing part.

[41901] VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1168 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41902] VGAM1168 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1168 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1168 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41903] The complementary binding of VGAM1168 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1168 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1168 host target RNA into VGAM1168 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41904] It is appreciated that VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1168 host target genes. The mRNA of each one of this plurality of VGAM1168 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1168 RNA, herein designated VGAM RNA, and which when bound by VGAM1168 RNA causes inhibition of translation of respective one or more VGAM1168 host target proteins.

[41905] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1168 gene, herein designated VGAM GENE, on one or more VGAM1168 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41906] It is yet further appreciated that a function of VGAM1168 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1168 correlate with, and may be deduced from, the identity of the host target genes which VGAM1168 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41907] Nucleotide sequences of the VGAM1168 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1168 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1168 are further described hereinbelow with reference to Table 1.

[41908] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1168 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1168 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41909] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1168 gene, herein designated VGAM is inhibition of expression of VGAM1168 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1168 correlate with, and may be deduced from, the identity of the target genes which VGAM1168 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41910] Interleukin 2 Receptor, Alpha (IL2RA, Accession NM_000417) is a VGAM1168 host target gene. IL2RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL2RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL2RA BINDING SITE, designated SEQ ID:5998, to the nucleotide sequence of VGAM1168 RNA, herein designated VGAM RNA, also designated SEQ ID:3879.

[41911] A function of VGAM1168 is therefore inhibition of Interleukin 2 Receptor, Alpha (IL2RA, Accession NM_000417), a gene which plays a role in T cell mediated immune response. Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL2RA. The function of IL2RA has been established by previous studies. The action of the T-cell growth factor interleukin-2 (IL2; 147680) requires the presence of a cell surface receptor. As most peripheral as well as thymic T cells do not carry the receptor in vivo, the regulated expression of IL2R appears to be a safeguard against a catastrophic spread of T-cell proliferation by an immunogenic stimulus. The receptor is a heterodimer, consisting of 1 alpha and 1 beta chain; the beta chain (OMIM Ref. No. 146710) was not characterized until 1989. The receptor molecule, a glycoprotein, has a relative mass of about 55,000. Its intracellular precursor is smaller. Leonard et al. (1983) used a monoclonal antibody for T-cell growth factor to characterize the receptor. Yang et al. (2001) analyzed T-cell subsets and levels of cytokine IL2 and soluble IL2 receptor in the peripheral blood of patients with normal pressure glaucoma (NPG; 606657) and primary open angle glaucoma (POAG;

137760) and compared them to values in age-matched controls. They found an increased frequency of CD8⁺/HLA-DR⁺ lymphocytes in patients with NPG and increased CD3⁺/CD8⁺ lymphocytes in both NPG and POAG patients. CD5⁺ lymphocytes were higher only in POAG patients. The mean concentration of soluble IL2R was higher in NPG and POAG patients than in controls although the IL2 concentration was similar in patients and controls. The authors concluded that the immune system might play an important role in initiation or progression of glaucomatous optic neuropathy in some patients.

[41912] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41913] Leonard, W. J.; Donlon, T. A.; Lebo, R. V.; Greene, W. C. : Localization of the gene encoding the human interleukin-2 receptor on chromosome 10. *Science* 228: 1547-1549, 1985. ; and

[41914] Yang, J.; Patil, R. V.; Yu, H.; Gordon, M.; Wax, M. B. : T cell subsets and sIL-2R/IL-2 levels in patients with glaucoma. *Am. J. Ophthal.* 131: 421-426, 2001.

[41915] Further studies establishing the function and utilities of IL2RA are found in John Hopkins OMIM database record ID

147730, and in cited publications numbered 11193–11201, 12009, 11264–11265, 680, 11266–1127 and 681 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184) is another VGAM1168 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31304, to the nucleotide sequence of VGAM1168 RNA, herein designated VGAM RNA, also designated SEQ ID:3879.

[41916] Another function of VGAM1168 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184). Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1. Tripartite Motif-containing 34 (TRIM34, Accession NM_021616) is another VGAM1168 host target gene. TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2 are

HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2, designated SEQ ID:22252 and SEQ ID:28176 respectively, to the nucleotide sequence of VGAM1168 RNA, herein designated VGAM RNA, also designated SEQ ID:3879.

[41917] Another function of VGAM1168 is therefore inhibition of Tripartite Motif-containing 34 (TRIM34, Accession NM_021616). Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM34. Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815) is another VGAM1168 host target gene. SLC5A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC5A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC5A7 BINDING SITE, designated SEQ ID:22386, to the nucleotide sequence of VGAM1168 RNA,

herein designated VGAM RNA, also designated SEQ ID:3879.

[41918] Another function of VGAM1168 is therefore inhibition of Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815). Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC5A7. LOC56959 (Accession XM_088578) is another VGAM1168 host target gene. LOC56959 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56959, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56959 BINDING SITE, designated SEQ ID:39840, to the nucleotide sequence of VGAM1168 RNA, herein designated VGAM RNA, also designated SEQ ID:3879.

[41919] Another function of VGAM1168 is therefore inhibition of LOC56959 (Accession XM_088578). Accordingly, utilities of VGAM1168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56959. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1169 (VGAM1169) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[41920] VGAM1169 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1169 was detected is described hereinabove with reference to Figs. 1–8.

[41921] VGAM1169 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rana Tigrina Ranavirus. VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[41922] VGAM1169 gene encodes a VGAM1169 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1169 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1169 precursor RNA is designated SEQ ID:1155, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1155 is located at position 92520 relative to the

genome of Rana Tigrina Ranavirus.

[41923] VGAM1169 precursor RNA folds onto itself, forming VGAM1169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[41924] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1169 folded precursor RNA into VGAM1169 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1169 RNA is designated SEQ ID:3880, and is provided hereinbelow with reference to the sequence listing part.

[41925] VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1169 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[41926] VGAM1169 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1169 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1169 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[41927] The complementary binding of VGAM1169 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1169 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1169 host target RNA into VGAM1169 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[41928] It is appreciated that VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1169 host target genes. The mRNA of each one of this plurality of VGAM1169 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1169 RNA, herein designated VGAM RNA, and which when bound by VGAM1169 RNA causes inhibition of translation of respective one or more VGAM1169 host target proteins.

[41929] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1169 gene, herein designated VGAM GENE, on one or more VGAM1169 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[41930] It is yet further appreciated that a function of VGAM1169 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGAM1169

correlate with, and may be deduced from, the identity of the host target genes which VGAM1169 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[41931] Nucleotide sequences of the VGAM1169 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1169 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1169 are further described hereinbelow with reference to Table 1.

[41932] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1169 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1169 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[41933] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1169 gene, herein designated VGAM is inhibition of expression of VGAM1169 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1169 correlate with, and may be deduced

from, the identity of the target genes which VGAM1169 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[41934] ACK1 (Accession NM_005781) is a VGAM1169 host target gene. ACK1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ACK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACK1 BINDING SITE, designated SEQ ID:12361, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41935] A function of VGAM1169 is therefore inhibition of ACK1 (Accession NM_005781). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACK1. A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139028) is another VGAM1169 host target gene. ADAMTS13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ADAMTS13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS13 BINDING SITE, designated SEQ ID:29130, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41936] Another function of VGAM1169 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139028), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS13. The function of ADAMTS13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Adenylate Cyclase 8 (brain) (ADCY8, Accession NM_001115) is another VGAM1169 host target gene. ADCY8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADCY8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ADCY8 BINDING SITE, designated SEQ ID:6789, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41937] Another function of VGAM1169 is therefore inhibition of Adenylate Cyclase 8 (brain) (ADCY8, Accession NM_001115), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY8. The function of ADCY8 has been established by previous studies. Adenylyl cyclase (EC 4.6.1.1) catalyzes the transformation of ATP into cyclic AMP. The enzymatic activity is under the control of several hormones, and different polypeptides participate in the transduction of the signal from the receptor to the catalytic moiety. Stimulatory or inhibitory receptors (R_s and R_i) interact with G proteins (G_s and G_i) that exhibit GTPase activity and they modulate the activity of the catalytic subunit of the adenylyl cyclase. Parma et al. (1991) cloned a cDNA corresponding to human brain adenylyl cyclase, symbolized by them as HBAC1. By in situ hybridization to metaphase chromosomal spreads using the human brain cDNA probe,

Stengel et al. (1992) showed that the gene is located on 8q24.2. A highly homologous gene, ADCY2 (OMIM Ref. No. 103071), was assigned to 5p15.3 by the same method.

[41938] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41939] Parma, J.; Stengel, D.; Gannage, M.–H.; Poyard, M.; Barouki, R.; Hanoune, J. : Sequence of a human brain adenylyl cyclase partial cDNA: evidence for a consensus cyclase domain. Biochem. Biophys. Res. Commun. 179: 455–462, 1991. ; and

[41940] Stengel, D.; Parma, J.; Gannage, M.–H.; Roeckel, N.; Mattei, M.–G.; Barouki, R.; Hanoune, J. : Different chromosomal localization of two adenylyl cyclase genes expressed in human brain.

[41941] Further studies establishing the function and utilities of ADCY8 are found in John Hopkins OMIM database record ID 103070, and in cited publications numbered 492–493 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cell Division Cycle 2–like 2 (CDC2L2, Accession NM_033532) is another VGAM1169 host target gene. CDC2L2 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDC2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC2L2 BINDING SITE, designated SEQ ID:27300, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41942] Another function of VGAM1169 is therefore inhibition of Cell Division Cycle 2-like 2 (CDC2L2, Accession NM_033532). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC2L2. Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372) is another VGAM1169 host target gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15025, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ

ID:3880.

[41943] Another function of VGAM1169 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. CAMP Responsive Element Binding Protein 1 (CREB1, Accession NM_004379) is another VGAM1169 host target gene. CREB1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CREB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREB1 BINDING SITE, designated SEQ ID:10601, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41944] Another function of VGAM1169 is therefore inhibition of CAMP Responsive Element Binding Protein 1 (CREB1, Ac-

cession NM_004379), a gene which regulates expression of cAMP-inducible genes. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREB1. The function of CREB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497.D Site of Albumin Promoter (albumin D-box) Binding Protein (DBP, Accession NM_001352) is another VGAM1169 host target gene. DBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBP BINDING SITE, designated SEQ ID:7031, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41945] Another function of VGAM1169 is therefore inhibition of D Site of Albumin Promoter (albumin D-box) Binding Protein (DBP, Accession NM_001352), a gene which generates macrophage-activating factor and enhances ingestion activity of macrophages. Accordingly, utilities of VGAM1169

include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBP. The function of DBP has been established by previous studies. Yamamoto and Homma (1991) presented evidence from studies in mice that vitamin D-3 binding protein is a precursor for the macrophage-activating factor, that it is converted by the membrane glycosidases of B and T cells to the macrophage-activating factor, and that enzymatic conversion of Gc protein to the macrophage-activating factor can occur in vitro. In vitro treatment of mouse peritoneal adherent cells (macrophages) alone with lysophosphatidylcholine or dodecylglycerol results in no enhanced ingestion activity of macrophages. However, incubation of peritoneal cells with these agents in serum-supplemented medium results in greatly enhanced phagocytic activity. Gc is the serum factor responsible for this. The role of Gc in this function suggests possible mechanisms for maintenance of the Gc polymorphism. Along with gelsolin (OMIM Ref. No. 137350), the Gc protein binds actin, which is released into the circulation with cell necrosis. This is the so-called extracellular actin-scavenger system which prevents toxic effects of actin. By immunoelectrophoresis, Hirschfeld (1959) discovered polymorphism of the serum

alpha-2-globulin called Gc for group-specific component. Gc1-1, Gc2-2, and Gc2-1 phenotypes can be distinguished also by starch or agar electrophoresis (Bearn et al., 1964). In the same year that Gc proteins were reported, another human plasma protein, vitamin D-binding alpha-globulin (VDBG), was described. Daiger et al. (1975) demonstrated that Gc and VDBG are identical. The worldwide polymorphism of Gc is now not surprising. Mourant et al. (1976) concluded that high frequency of the Gc(2) allele corresponds, with some exceptions, to low levels of sunlight. Within Ireland, the correlation did not hold. By a novel method of labeling Gc protein with radioactive vitamin D, followed with electrophoresis and autoradiography, Daiger and Cavalli-Sforza (1977) detected new Gc variants. The gene frequency of some of the variants was as high as 15%. They were testing a physiologically relevant property of the Gc protein. In Iceland, Karlsson et al. (1980) used immunofixation electrophoresis for Gc typing according to the method of Johnson et al. (1975). They found a new variant first thought to be identical to Gc Norway but later shown to be distinct.

[41946] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [41947] Kofler, A.; Braun, A.; Jenkins, T.; Serjeantson, S. W.; Cleve, H. : Characterization of mutants of the vitamin-D-binding protein/group specific component: GC Aborigine (1A1) from Australian Aborigines and South African blacks, and 2A9 from South Germany. *Vox Sang.* 68: 50–54, 1995. ; and
- [41948] Yamamoto, N.; Homma, S. : Vitamin D-3 binding protein (group-specific component) is a precursor for the macrophage-activating signal factor from lysophosphatidylcholine-treated lymphocy.
- [41949] Further studies establishing the function and utilities of DBP are found in John Hopkins OMIM database record ID 139200, and in cited publications numbered 1563–1564, 3785–1567, 3063–3087, 3652–3094, 3362, 378 and 3363–3379 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.Deleted
In Lung and Esophageal Cancer 1 (DLEC1, Accession NM_007336) is another VGAM1169 host target gene.
DLEC1 BINDING SITE1 and DLEC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DLEC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLEC1 BINDING SITE1 and DLEC1 BINDING SITE2, designated SEQ ID:14266 and SEQ ID:14273 respectively, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41950] Another function of VGAM1169 is therefore inhibition of Deleted In Lung and Esophageal Cancer 1 (DLEC1, Accession NM_007336). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLEC1. Dishevelled, Dsh Homolog 1 (Drosophila) (DVL1, Accession XM_001589) is another VGAM1169 host target gene. DVL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL1 BINDING SITE, designated SEQ ID:29844, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41951] Another function of VGAM1169 is therefore inhibition of Dishevelled, Dsh Homolog 1 (Drosophila) (DVL1, Acces-

sion XM_001589), a gene which may play a role in the signal transduction pathway . Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL1. The function of DVL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Frizzled-related Protein (FRZB, Accession NM_001463) is another VGAM1169 host target gene. FRZB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FRZB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRZB BINDING SITE, designated SEQ ID:7198, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41952] Another function of VGAM1169 is therefore inhibition of Frizzled-related Protein (FRZB, Accession NM_001463), a gene which may be involved in morphogenesis of skeleton. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FRZB. The function of FRZB has been

established by previous studies. Transplantation experiments by Spemann and Mangold (1924) established the presence of an anatomically discrete region, the Spemann organizer, or dorsal lip, that controls patterning of the developing body axis in vertebrate embryos. Diffusible factors emanating from this region, such as 'goosecoid' (GSC; 138890) and 'noggin' (NOG; 602991), regulate skeletal morphogenesis. *Drosophila* cuticle hairs are arranged in a defined polarity that is genetically controlled by 'frizzled' (see OMIM Ref. No. FZD1; 603408), a 7-transmembrane receptor with a large extracellular cysteine-rich domain (CRD).

[41953] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[41954] Leyns, L.; Bouwmeester, T.; Kim, S.-H.; Piccolo, S.; De Robertis, E. M. : Frzb-1 is a secreted antagonist of Wnt signaling expressed in the Spemann organizer. *Cell* 88: 747-756, 1997. ; and

[41955] Spemann, H.; Mangold, H. : Ueber induktion von embryonalanlagen durch implantation artfremder organisatoren. *Arch. Mikroskopische Anat. Entwicklungsmechanik* 100: 599-638, 1924.

[41956] Further studies establishing the function and utilities of FRZB are found in John Hopkins OMIM database record ID 605083, and in cited publications numbered 6601–6603, 42 and 6604 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Frizzled Homolog 8 (Drosophila) (FZD8, Accession NM_031866) is another VGAM1169 host target gene. FZD8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD8 BINDING SITE, designated SEQ ID:25625, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41957] Another function of VGAM1169 is therefore inhibition of Frizzled Homolog 8 (Drosophila) (FZD8, Accession NM_031866), a gene which may be involved in transduction and intercellular transmission of polarity information during tissue morphogenesis and/or in differentiated tissues. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD8. The function of FZD8 and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM503. Growth Arrest-specific 7 (GAS7, Accession NM_003644) is another VGAM1169 host target gene. GAS7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAS7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS7 BINDING SITE, designated SEQ ID:9717, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41958] Another function of VGAM1169 is therefore inhibition of Growth Arrest-specific 7 (GAS7, Accession NM_003644), a gene which may play a role in promoting maturation and morphological differentiation of cerebellar neurons. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS7. The function of GAS7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Gap Junction Protein,

Beta 3, 31kDa (connexin 31) (GJB3, Accession NM_024009) is another VGAM1169 host target gene. GJB3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GJB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJB3 BINDING SITE, designated SEQ ID:23440, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41959] Another function of VGAM1169 is therefore inhibition of Gap Junction Protein, Beta 3, 31kDa (connexin 31) (GJB3, Accession NM_024009). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJB3. Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM_031899) is another VGAM1169 host target gene. GORASP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GORASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GORASP1 BINDING SITE, designated

SEQ ID:25647, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41960] Another function of VGAM1169 is therefore inhibition of Golgi Reassembly Stacking Protein 1, 65kDa (GORASP1, Accession NM_031899), a gene which has some function with the Golgi apparatus. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GORASP1. The function of GORASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM630. Leucine Zipper Protein 1 (LUZP1, Accession NM_033631) is another VGAM1169 host target gene. LUZP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LUZP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LUZP1 BINDING SITE, designated SEQ ID:27350, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41961] Another function of VGAM1169 is therefore inhibition of Leucine Zipper Protein 1 (LUZP1, Accession NM_033631). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LUZP1. Matrix Metalloproteinase 8 (neutrophil collagenase) (MMP8, Accession NM_002424) is another VGAM1169 host target gene. MMP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP8 BINDING SITE, designated SEQ ID:8259, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41962] Another function of VGAM1169 is therefore inhibition of Matrix Metalloproteinase 8 (neutrophil collagenase) (MMP8, Accession NM_002424). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP8. Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM_000530) is another VGAM1169 host target gene. MPZ BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by MPZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPZ BINDING SITE, designated SEQ ID:6131, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41963] Another function of VGAM1169 is therefore inhibition of Myelin Protein Zero (Charcot-Marie-Tooth neuropathy 1B) (MPZ, Accession NM_000530). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPZ. Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Beta Polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55) (P4HB, Accession NM_000918) is another VGAM1169 host target gene. P4HB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P4HB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P4HB BINDING SITE, designated SEQ ID:6629, to the nucleotide sequence of VGAM1169 RNA,

herein designated VGAM RNA, also designated SEQ ID:3880.

[41964] Another function of VGAM1169 is therefore inhibition of Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Beta Polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55) (P4HB, Accession NM_000918), a gene which catalyzes formation of 4-hydroxyproline in collagens. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P4HB. The function of P4HB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM589. RAD54B (Accession NM_134434) is another VGAM1169 host target gene. RAD54B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAD54B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD54B BINDING SITE, designated SEQ ID:28677, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41965] Another function of VGAM1169 is therefore inhibition of RAD54B (Accession NM_134434), a gene which is involved in dna repair and mitotic recombination. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD54B. The function of RAD54B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM_014781) is another VGAM1169 host target gene. RB1CC1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RB1CC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RB1CC1 BINDING SITE, designated SEQ ID:16631, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41966] Another function of VGAM1169 is therefore inhibition of RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM_014781), a gene which is likely to participate in nuclear architecture by connecting chromatin with the nu-

clear matrix or envelope. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RB1CC1. The function of RB1CC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18. Reelin (RELN, Accession XM_168628) is another VGAM1169 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45278, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41967] Another function of VGAM1169 is therefore inhibition of Reelin (RELN, Accession XM_168628), a gene which regulates microtubule function in neurons and neuronal migration. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM35.SRY (sex determining region Y)-box 4 (SOX4, Accession

NM_003107) is another VGAM1169 host target gene.

SOX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX4 BINDING SITE, designated SEQ ID:9075, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41968] Another function of VGAM1169 is therefore inhibition of SRY (sex determining region Y)-box 4 (SOX4, Accession NM_003107), a gene which binds with high affinity to the t-cell enhancer motif 5'-aacaag-3' motif. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX4. The function of SOX4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM409.Stanniocalcin 1 (STC1, Accession NM_003155) is another VGAM1169 host target gene.

STC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STC1 BINDING SITE, designated SEQ ID:9136, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41969] Another function of VGAM1169 is therefore inhibition of Stanniocalcin 1 (STC1, Accession NM_003155), a gene which stimulates renal phosphate reabsorption, and could therefore prevent hypercalcemia. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STC1. The function of STC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM623. Transforming Growth Factor, Alpha (TGFA, Accession NM_003236) is another VGAM1169 host target gene. TGFA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of TGFA BINDING SITE, designated SEQ ID:9231, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41970] Another function of VGAM1169 is therefore inhibition of Transforming Growth Factor, Alpha (TGFA, Accession NM_003236), a gene which is able to bind to the egf receptor and to act synergistically with tgfbeta to promote anchorage-independent cell proliferation in soft agar. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFA. The function of TGFA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM328. T-cell Lymphoma Invasion and Metastasis 1 (TIAM1, Accession NM_003253) is another VGAM1169 host target gene. TIAM1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAM1 BINDING SITE, designated SEQ ID:9261, to the nucleotide se-

quence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41971] Another function of VGAM1169 is therefore inhibition of T-cell Lymphoma Invasion and Metastasis 1 (TIAM1, Accession NM_003253), a gene which modulates the activity of Rho-like proteins and connects extracellular signals to cytoskeletal activities. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAM1. The function of TIAM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1098. Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257) is another VGAM1169 host target gene. TJP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TJP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TJP1 BINDING SITE, designated SEQ ID:9265, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41972] Another function of VGAM1169 is therefore inhibition of

Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257), a gene which colocalizes and interacts with cadherins in cells lacking tight junctions. Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TJP1. The function of TJP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. A Kinase (PRKA) Anchor Protein 8 (AKAP8, Accession NM_005858) is another VGAM1169 host target gene. AKAP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP8 BINDING SITE, designated SEQ ID:12465, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41973] Another function of VGAM1169 is therefore inhibition of A Kinase (PRKA) Anchor Protein 8 (AKAP8, Accession NM_005858). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with AKAP8. Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM_001716) is another VGAM1169 host target gene. BLR1 BINDING SITE1 and BLR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BLR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLR1 BINDING SITE1 and BLR1 BINDING SITE2, designated SEQ ID:7447 and SEQ ID:26777 respectively, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41974] Another function of VGAM1169 is therefore inhibition of Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM_001716). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLR1. Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289) is another VGAM1169 host target gene. CLIC2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CLIC2, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC2 BINDING SITE, designated SEQ ID:6967, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41975] Another function of VGAM1169 is therefore inhibition of Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC2. Cyclin M2 (CNNM2, Accession NM_017649) is another VGAM1169 host target gene. CNNM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM2 BINDING SITE, designated SEQ ID:19155, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41976] Another function of VGAM1169 is therefore inhibition of Cyclin M2 (CNNM2, Accession NM_017649). Accordingly,

utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM2. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681) is another VGAM1169 host target gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16165, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41977] Another function of VGAM1169 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 35 (DDX35, Accession NM_021931) is another VGAM1169 host target gene. DDX35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX35, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX35 BINDING SITE, designated SEQ ID:22454, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41978] Another function of VGAM1169 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 35 (DDX35, Accession NM_021931). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX35. DKFZP434L187 (Accession XM_044070) is another VGAM1169 host target gene. DKFZP434L187 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434L187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L187 BINDING SITE, designated SEQ ID:34121, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41979] Another function of VGAM1169 is therefore inhibition of

DKFZP434L187 (Accession XM_044070). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L187. DKFZP434N178 (Accession XM_050278) is another VGAM1169 host target gene. DKFZP434N178 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434N178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N178 BINDING SITE, designated SEQ ID:35598, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41980] Another function of VGAM1169 is therefore inhibition of DKFZP434N178 (Accession XM_050278). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N178. DKFZP586I2223 (Accession NM_015438) is another VGAM1169 host target gene. DKFZP586I2223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586I2223, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586I2223 BINDING SITE, designated SEQ ID:17732, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41981] Another function of VGAM1169 is therefore inhibition of DKFZP586I2223 (Accession NM_015438). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586I2223. FLJ13710 (Accession NM_024817) is another VGAM1169 host target gene. FLJ13710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13710 BINDING SITE, designated SEQ ID:24206, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41982] Another function of VGAM1169 is therefore inhibition of FLJ13710 (Accession NM_024817). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13710. FLJ20154 (Accession XM_053688) is another VGAM1169 host target gene. FLJ20154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20154 BINDING SITE, designated SEQ ID:36106, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41983] Another function of VGAM1169 is therefore inhibition of FLJ20154 (Accession XM_053688). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20154. GS3955 (Accession NM_021643) is another VGAM1169 host target gene. GS3955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GS3955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GS3955 BINDING SITE, designated SEQ ID:22305, to the nucleotide

sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41984] Another function of VGAM1169 is therefore inhibition of GS3955 (Accession NM_021643). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GS3955. KIAA0296 (Accession NM_014699) is another VGAM1169 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16222, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41985] Another function of VGAM1169 is therefore inhibition of KIAA0296 (Accession NM_014699). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. KIAA0337 (Accession NM_014786) is another VGAM1169 host target gene. KIAA0337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0337 BINDING SITE, designated SEQ ID:16655, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41986] Another function of VGAM1169 is therefore inhibition of KIAA0337 (Accession NM_014786). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0337. KIAA0415 (Accession XM_166527) is another VGAM1169 host target gene. KIAA0415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0415 BINDING SITE, designated SEQ ID:44477, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41987] Another function of VGAM1169 is therefore inhibition of KIAA0415 (Accession XM_166527). Accordingly, utilities

of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0415. KIAA0472 (Accession XM_050147) is another VGAM1169 host target gene. KIAA0472 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0472 BINDING SITE, designated SEQ ID:35580, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41988] Another function of VGAM1169 is therefore inhibition of KIAA0472 (Accession XM_050147). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0472. KIAA0668 (Accession XM_039332) is another VGAM1169 host target gene. KIAA0668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0668 BINDING SITE, designated SEQ ID:33053, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41989] Another function of VGAM1169 is therefore inhibition of KIAA0668 (Accession XM_039332). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0668. KIAA1023 (Accession NM_017604) is another VGAM1169 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19090, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41990] Another function of VGAM1169 is therefore inhibition of KIAA1023 (Accession NM_017604). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. KIAA1184 (Accession NM_022572) is another VGAM1169 host target gene. KIAA1184 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1184 BINDING SITE, designated SEQ ID:22893, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41991] Another function of VGAM1169 is therefore inhibition of KIAA1184 (Accession NM_022572). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1184. KIAA1374 (Accession XM_028413) is another VGAM1169 host target gene. KIAA1374 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1374, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1374 BINDING SITE, designated SEQ ID:30709, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41992] Another function of VGAM1169 is therefore inhibition of

KIAA1374 (Accession XM_028413). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1374. KIAA1464 (Accession XM_043069) is another VGAM1169 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33884, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41993] Another function of VGAM1169 is therefore inhibition of KIAA1464 (Accession XM_043069). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1464. KIAA1674 (Accession XM_044065) is another VGAM1169 host target gene. KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34113, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41994] Another function of VGAM1169 is therefore inhibition of KIAA1674 (Accession XM_044065). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. LPS-responsive Vesicle Trafficking, Beach and Anchor Containing (LRBA, Accession NM_006726) is another VGAM1169 host target gene. LRBA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRBA BINDING SITE, designated SEQ ID:13557, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41995] Another function of VGAM1169 is therefore inhibition of LPS-responsive Vesicle Trafficking, Beach and Anchor Containing (LRBA, Accession NM_006726). Accordingly, utilities of VGAM1169 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with LRBA. MAGE-E1 (Accession NM_030801) is another VGAM1169 host target gene. MAGE-E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAGE-E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGE-E1 BINDING SITE, designated SEQ ID:25108, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41996] Another function of VGAM1169 is therefore inhibition of MAGE-E1 (Accession NM_030801). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGE-E1. MDS006 (Accession NM_020233) is another VGAM1169 host target gene. MDS006 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDS006, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDS006 BINDING SITE, designated SEQ ID:21502, to the nucleotide

sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41997] Another function of VGAM1169 is therefore inhibition of MDS006 (Accession NM_020233). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDS006. MGC2663 (Accession NM_024106) is another VGAM1169 host target gene. MGC2663 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2663 BINDING SITE, designated SEQ ID:23551, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41998] Another function of VGAM1169 is therefore inhibition of MGC2663 (Accession NM_024106). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2663. MGC33371 (Accession NM_144664) is another VGAM1169 host target gene. MGC33371 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by MGC33371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC33371 BINDING SITE, designated SEQ ID:29480, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[41999] Another function of VGAM1169 is therefore inhibition of MGC33371 (Accession NM_144664). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC33371. MAP Kinase-interacting Serine/threonine Kinase 1 (MKNK1, Accession NM_003684) is another VGAM1169 host target gene. MKNK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MKNK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKNK1 BINDING SITE, designated SEQ ID:9794, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42000] Another function of VGAM1169 is therefore inhibition of

MAP Kinase–interacting Serine/threonine Kinase 1 (MKNK1, Accession NM_003684). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKNK1. Matrix Metalloproteinase–like 1 (MMPL1, Accession NM_004142) is another VGAM1169 host target gene. MMPL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMPL1 BINDING SITE, designated SEQ ID:10348, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42001] Another function of VGAM1169 is therefore inhibition of Matrix Metalloproteinase–like 1 (MMPL1, Accession NM_004142). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMPL1. N4BP3 (Accession XM_038920) is another VGAM1169 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by N4BP3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32930, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42002] Another function of VGAM1169 is therefore inhibition of N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. NAG14 (Accession NM_022143) is another VGAM1169 host target gene. NAG14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAG14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAG14 BINDING SITE, designated SEQ ID:22705, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42003] Another function of VGAM1169 is therefore inhibition of NAG14 (Accession NM_022143). Accordingly, utilities of

VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAG14. PIP3-E (Accession XM_039749) is another VGAM1169 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33180, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42004] Another function of VGAM1169 is therefore inhibition of PIP3-E (Accession XM_039749). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792) is another VGAM1169 host target gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of PTPNS1 BINDING SITE, designated SEQ ID:28055, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42005] Another function of VGAM1169 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. RAN Binding Protein 8 (RANBP8, Accession NM_006390) is another VGAM1169 host target gene. RANBP8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RANBP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RANBP8 BINDING SITE, designated SEQ ID:13094, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42006] Another function of VGAM1169 is therefore inhibition of RAN Binding Protein 8 (RANBP8, Accession NM_006390). Accordingly, utilities of VGAM1169 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with RANBP8. Small Nuclear Ribonucleoprotein D1 Polypeptide 16kDa (SNRPD1, Accession NM_006938) is another VGAM1169 host target gene. SNRPD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNRPD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNRPD1 BINDING SITE, designated SEQ ID:13821, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42007] Another function of VGAM1169 is therefore inhibition of Small Nuclear Ribonucleoprotein D1 Polypeptide 16kDa (SNRPD1, Accession NM_006938). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNRPD1. TED (Accession NM_015686) is another VGAM1169 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17920, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42008] Another function of VGAM1169 is therefore inhibition of TED (Accession NM_015686). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. TU12B1-TY (Accession NM_016575) is another VGAM1169 host target gene. TU12B1-TY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU12B1-TY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU12B1-TY BINDING SITE, designated SEQ ID:18648, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42009] Another function of VGAM1169 is therefore inhibition of TU12B1-TY (Accession NM_016575). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

TU12B1-TY. UBCE7IP5 (Accession NM_014948) is another VGAM1169 host target gene. UBCE7IP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBCE7IP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBCE7IP5 BINDING SITE, designated SEQ ID:17273, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42010] Another function of VGAM1169 is therefore inhibition of UBCE7IP5 (Accession NM_014948). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBCE7IP5. LOC127294 (Accession XM_059131) is another VGAM1169 host target gene. LOC127294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127294 BINDING SITE, designated SEQ ID:36894, to the nucleotide sequence of VGAM1169 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3880.

[42011] Another function of VGAM1169 is therefore inhibition of LOC127294 (Accession XM_059131). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127294. LOC129676 (Accession XM_065341) is another VGAM1169 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37285, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42012] Another function of VGAM1169 is therefore inhibition of LOC129676 (Accession XM_065341). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129676. LOC138389 (Accession XM_072534) is another VGAM1169 host target gene. LOC138389 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC138389, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138389 BINDING SITE, designated SEQ ID:37507, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42013] Another function of VGAM1169 is therefore inhibition of LOC138389 (Accession XM_072534). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138389. LOC144970 (Accession XM_084998) is another VGAM1169 host target gene. LOC144970 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144970 BINDING SITE, designated SEQ ID:37793, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42014] Another function of VGAM1169 is therefore inhibition of LOC144970 (Accession XM_084998). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC144970. LOC145623 (Accession XM_096822) is another VGAM1169 host target gene. LOC145623 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145623 BINDING SITE, designated SEQ ID:40545, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42015] Another function of VGAM1169 is therefore inhibition of LOC145623 (Accession XM_096822). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145623. LOC146520 (Accession XM_085492) is another VGAM1169 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38186, to

the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42016] Another function of VGAM1169 is therefore inhibition of LOC146520 (Accession XM_085492). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC147912 (Accession XM_085952) is another VGAM1169 host target gene. LOC147912 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147912 BINDING SITE, designated SEQ ID:38418, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42017] Another function of VGAM1169 is therefore inhibition of LOC147912 (Accession XM_085952). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147912. LOC148946 (Accession XM_097557) is another VGAM1169 host target gene. LOC148946 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC148946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148946 BINDING SITE, designated SEQ ID:40940, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42018] Another function of VGAM1169 is therefore inhibition of LOC148946 (Accession XM_097557). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148946. LOC151009 (Accession XM_097992) is another VGAM1169 host target gene. LOC151009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151009 BINDING SITE, designated SEQ ID:41289, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42019] Another function of VGAM1169 is therefore inhibition of LOC151009 (Accession XM_097992). Accordingly, utilities

of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151009. LOC152283 (Accession XM_098196) is another VGAM1169 host target gene. LOC152283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152283 BINDING SITE, designated SEQ ID:41487, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42020] Another function of VGAM1169 is therefore inhibition of LOC152283 (Accession XM_098196). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152283. LOC155179 (Accession XM_088169) is another VGAM1169 host target gene. LOC155179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC155179 BINDING SITE, designated SEQ ID:39557, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42021] Another function of VGAM1169 is therefore inhibition of LOC155179 (Accession XM_088169). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155179. LOC164714 (Accession XM_104657) is another VGAM1169 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42182, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42022] Another function of VGAM1169 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC196047 (Accession XM_116883) is another VGAM1169 host target gene. LOC196047 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196047 BINDING SITE, designated SEQ ID:43143, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42023] Another function of VGAM1169 is therefore inhibition of LOC196047 (Accession XM_116883). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196047. LOC196472 (Accession XM_113727) is another VGAM1169 host target gene. LOC196472 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196472 BINDING SITE, designated SEQ ID:42375, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42024] Another function of VGAM1169 is therefore inhibition of

LOC196472 (Accession XM_113727). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196472. LOC199858 (Accession XM_114040) is another VGAM1169 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42639, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42025] Another function of VGAM1169 is therefore inhibition of LOC199858 (Accession XM_114040). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC200597 (Accession XM_114266) is another VGAM1169 host target gene. LOC200597 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC200597 BINDING SITE, designated SEQ ID:42825, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42026] Another function of VGAM1169 is therefore inhibition of LOC200597 (Accession XM_114266). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200597. LOC203636 (Accession XM_114868) is another VGAM1169 host target gene. LOC203636 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203636, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203636 BINDING SITE, designated SEQ ID:43077, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42027] Another function of VGAM1169 is therefore inhibition of LOC203636 (Accession XM_114868). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203636. LOC219686 (Accession XM_165544) is an-

other VGAM1169 host target gene. LOC219686 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219686 BINDING SITE, designated SEQ ID:43674, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42028] Another function of VGAM1169 is therefore inhibition of LOC219686 (Accession XM_165544). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219686. LOC219899 (Accession XM_166173) is another VGAM1169 host target gene. LOC219899 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219899 BINDING SITE, designated SEQ ID:43989, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42029] Another function of VGAM1169 is therefore inhibition of LOC219899 (Accession XM_166173). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219899. LOC220018 (Accession XM_167816) is another VGAM1169 host target gene. LOC220018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220018 BINDING SITE, designated SEQ ID:44856, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42030] Another function of VGAM1169 is therefore inhibition of LOC220018 (Accession XM_167816). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220018. LOC220906 (Accession XM_166133) is another VGAM1169 host target gene. LOC220906 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220906, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220906 BINDING SITE, designated SEQ ID:43926, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42031] Another function of VGAM1169 is therefore inhibition of LOC220906 (Accession XM_166133). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220906. LOC222486 (Accession XM_169432) is another VGAM1169 host target gene. LOC222486 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222486 BINDING SITE, designated SEQ ID:45300, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42032] Another function of VGAM1169 is therefore inhibition of LOC222486 (Accession XM_169432). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC222486. LOC254532 (Accession XM_172961) is another VGAM1169 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46212, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42033] Another function of VGAM1169 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC256950 (Accession XM_170922) is another VGAM1169 host target gene. LOC256950 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256950 BINDING SITE, designated SEQ ID:45701, to the nucleotide sequence of VGAM1169 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3880.

[42034] Another function of VGAM1169 is therefore inhibition of LOC256950 (Accession XM_170922). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256950. LOC92299 (Accession XM_044075) is another VGAM1169 host target gene. LOC92299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92299 BINDING SITE, designated SEQ ID:34131, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42035] Another function of VGAM1169 is therefore inhibition of LOC92299 (Accession XM_044075). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92299. LOC92973 (Accession XM_048529) is another VGAM1169 host target gene. LOC92973 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92973, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92973 BINDING SITE, designated SEQ ID:35185, to the nucleotide sequence of VGAM1169 RNA, herein designated VGAM RNA, also designated SEQ ID:3880.

[42036] Another function of VGAM1169 is therefore inhibition of LOC92973 (Accession XM_048529). Accordingly, utilities of VGAM1169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92973. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1170 (VGAM1170) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42037] VGAM1170 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1170 was detected is described hereinabove with reference to Figs. 1-8.

[42038] VGAM1170 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Melanoplus Sanguinipes*

Entomopoxvirus. VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42039] VGAM1170 gene encodes a VGAM1170 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1170 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1170 precursor RNA is designated SEQ ID:1156, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1156 is located at position 35824 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[42040] VGAM1170 precursor RNA folds onto itself, forming VGAM1170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42041] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1170 folded precursor RNA into VGAM1170 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1170 RNA is designated SEQ ID:3881, and is provided hereinbelow with reference to the sequence listing part.

[42042] VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1170 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42043] VGAM1170 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1170 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1170 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42044] The complementary binding of VGAM1170 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1170 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1170 host target RNA into VGAM1170 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42045] It is appreciated that VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1170 host target genes. The mRNA of each one of this plurality of VGAM1170 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1170 RNA, herein designated VGAM RNA, and which when bound by VGAM1170 RNA causes inhibition of translation of respective one or more VGAM1170 host target proteins.

[42046] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1170 gene, herein designated VGAM GENE, on one or more VGAM1170 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42047] It is yet further appreciated that a function of VGAM1170 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1170 correlate with, and may be deduced from, the identity of the host target genes which VGAM1170 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42048] Nucleotide sequences of the VGAM1170 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1170 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1170 are further described hereinbelow with reference to Table 1.

[42049] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1170 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1170 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42050] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1170 gene, herein designated VGAM is inhibition of expression of VGAM1170 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1170 correlate with, and may be deduced from, the identity of the target genes which VGAM1170 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42051] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_033173) is a VGAM1170 host target gene. B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5, designated SEQ ID:27037, SEQ ID:12699, SEQ ID:27022, SEQ ID:27027 and SEQ ID:27032 respectively, to the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, also designated SEQ ID:3881.

[42052] A function of VGAM1170 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_033173). Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT5. DKFZP434L187 (Accession XM_044070) is another VGAM1170 host target gene. DKFZP434L187 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434L187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L187 BINDING SITE, designated SEQ ID:34118, to the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, also designated SEQ ID:3881.

[42053] Another function of VGAM1170 is therefore inhibition of

DKFZP434L187 (Accession XM_044070). Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L187. NCUBE1 (Accession NM_016021) is another VGAM1170 host target gene. NCUBE1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCUBE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCUBE1 BINDING SITE, designated SEQ ID:18092, to the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, also designated SEQ ID:3881.

[42054] Another function of VGAM1170 is therefore inhibition of NCUBE1 (Accession NM_016021). Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCUBE1. LOC145773 (Accession XM_085237) is another VGAM1170 host target gene. LOC145773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC145773 BINDING SITE, designated SEQ ID:37983, to the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, also designated SEQ ID:3881.

[42055] Another function of VGAM1170 is therefore inhibition of LOC145773 (Accession XM_085237). Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145773. LOC145899 (Accession XM_096899) is another VGAM1170 host target gene. LOC145899 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145899 BINDING SITE, designated SEQ ID:40623, to the nucleotide sequence of VGAM1170 RNA, herein designated VGAM RNA, also designated SEQ ID:3881.

[42056] Another function of VGAM1170 is therefore inhibition of LOC145899 (Accession XM_096899). Accordingly, utilities of VGAM1170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145899. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1171 (VGAM1171) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42057] VGAM1171 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1171 was detected is described hereinabove with reference to Figs. 1–8.

[42058] VGAM1171 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cucumber Fruit Mottle Mosaic Virus. VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42059] VGAM1171 gene encodes a VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1171 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1171 precursor RNA is designated SEQ ID:1157, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1157 is located at position 4341 relative to the genome of Cucumber Fruit Mottle Mosaic Virus.

[42060] VGAM1171 precursor RNA folds onto itself, forming VGAM1171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42061] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1171 folded precursor RNA into VGAM1171 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1171 RNA is designated SEQ ID:3882, and is provided hereinbelow with reference to the sequence listing part.

[42062] VGAM1171 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1171 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42063] VGAM1171 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1171 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1171 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1171 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[42064] The complementary binding of VGAM1171 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1171 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1171 host target RNA into VGAM1171 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42065] It is appreciated that VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1171 host target genes. The mRNA of each one of this plurality of VGAM1171 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1171 RNA, herein designated VGAM RNA, and which when bound by VGAM1171 RNA causes inhibition of translation of respective one or more

VGAM1171 host target proteins.

[42066] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1171 gene, herein designated VGAM GENE, on one or more VGAM1171 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42067] It is yet further appreciated that a function of VGAM1171 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of viral infection by Cucumber Fruit Mottle Mo-

saic Virus. Specific functions, and accordingly utilities, of VGAM1171 correlate with, and may be deduced from, the identity of the host target genes which VGAM1171 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42068] Nucleotide sequences of the VGAM1171 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1171 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1171 are further described hereinbelow with reference to Table 1.

[42069] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1171 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1171 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42070] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1171 gene, herein designated VGAM is inhibition of expression of VGAM1171 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1171 correlate with, and may be deduced from, the identity of the target genes which VGAM1171 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42071] AXL Receptor Tyrosine Kinase (AXL, Accession NM_001699) is a VGAM1171 host target gene. AXL BINDING SITE1 and AXL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AXL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXL BINDING SITE1 and AXL BINDING SITE2, designated SEQ ID:7418 and SEQ ID:22439 respectively, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42072] A function of VGAM1171 is therefore inhibition of AXL Receptor Tyrosine Kinase (AXL, Accession NM_001699). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXL. Regulator of G-protein Signalling 5 (RGS5, Accession NM_003617) is another VGAM1171 host target gene. RGS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by RGS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS5 BINDING SITE, designated SEQ ID:9677, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42073] Another function of VGAM1171 is therefore inhibition of Regulator of G-protein Signalling 5 (RGS5, Accession NM_003617). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS5. KIAA0298 (Accession XM_084529) is another VGAM1171 host target gene. KIAA0298 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0298, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0298 BINDING SITE, designated SEQ ID:37624, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42074] Another function of VGAM1171 is therefore inhibition of

KIAA0298 (Accession XM_084529). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0298. KIAA1229 (Accession XM_030665) is another VGAM1171 host target gene. KIAA1229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1229 BINDING SITE, designated SEQ ID:31094, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42075] Another function of VGAM1171 is therefore inhibition of KIAA1229 (Accession XM_030665). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1229. LOC129607 (Accession XM_059368) is another VGAM1171 host target gene. LOC129607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC129607 BINDING SITE, designated SEQ ID:36972, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42076] Another function of VGAM1171 is therefore inhibition of LOC129607 (Accession XM_059368). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129607. LOC130639 (Accession XM_059464) is another VGAM1171 host target gene. LOC130639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130639 BINDING SITE, designated SEQ ID:37001, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42077] Another function of VGAM1171 is therefore inhibition of LOC130639 (Accession XM_059464). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130639. LOC200339 (Accession XM_117226) is an-

other VGAM1171 host target gene. LOC200339 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200339 BINDING SITE, designated SEQ ID:43297, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42078] Another function of VGAM1171 is therefore inhibition of LOC200339 (Accession XM_117226). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200339. LOC257465 (Accession XM_088384) is another VGAM1171 host target gene. LOC257465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257465 BINDING SITE, designated SEQ ID:39664, to the nucleotide sequence of VGAM1171 RNA, herein designated VGAM RNA, also designated SEQ ID:3882.

[42079] Another function of VGAM1171 is therefore inhibition of LOC257465 (Accession XM_088384). Accordingly, utilities of VGAM1171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257465. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1172 (VGAM1172) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42080] VGAM1172 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1172 was detected is described hereinabove with reference to Figs. 1–8.

[42081] VGAM1172 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cucumber Fruit Mottle Mosaic Virus. VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42082] VGAM1172 gene encodes a VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1172 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1172 precursor RNA is designated SEQ ID:1158, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1158 is located at position 5778 relative to the genome of Cucumber Fruit Mottle Mosaic Virus.

[42083] VGAM1172 precursor RNA folds onto itself, forming VGAM1172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42084] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1172 folded precursor RNA into VGAM1172 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1172 RNA is designated SEQ ID:3883, and is provided hereinbelow with reference to the sequence listing part.

[42085] VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1172 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[42086] VGAM1172 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1172 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1172 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42087] The complementary binding of VGAM1172 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1172 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1172 host target RNA into VGAM1172 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42088] It is appreciated that VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1172 host target genes. The mRNA of each one of this plurality of VGAM1172 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1172 RNA, herein designated VGAM RNA, and which when bound by VGAM1172 RNA causes inhibition of translation of respective one or more VGAM1172 host target proteins.

[42089] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1172 gene, herein designated VGAM GENE, on one or more VGAM1172 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42090] It is yet further appreciated that a function of VGAM1172 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of viral infection by Cucumber Fruit Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1172 correlate with, and may be deduced from, the identity of the host target genes which VGAM1172 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42091] Nucleotide sequences of the VGAM1172 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1172 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1172 are further described hereinbelow with reference to Table 1.

[42092] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1172 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1172 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[42093] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1172 gene, herein designated VGAM is inhibition of expression of VGAM1172 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1172 correlate with, and may be deduced from, the identity of the target genes which VGAM1172 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42094] F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM_012158) is a VGAM1172 host target gene. FBXL3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL3A BINDING SITE, designated SEQ ID:14456, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42095] A function of VGAM1172 is therefore inhibition of F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM_012158), a gene which is a putative SCF ubiquitin lig-

ase subunit involved in protein degradation. Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL3A. The function of FBXL3A has been established by previous studies. The F box, named after cyclin F (CCNF; 600227), in which it was originally observed, is an approximately 40–amino acid motif that binds SKP1 (OMIM Ref. No. 601434). F–box proteins are components of modular E3 ubiquitin protein ligases called SCFs (SKP1, OMIM Ref. No. 603134, F–box proteins), which function in phosphorylation–dependent ubiquitination. Using a yeast 2–hybrid screen with SKP1 as bait, followed by searching sequence databases, Winston et al. (1999) and Cenciarelli et al. (1999) identified 33 mammalian and 26 human F–box proteins, respectively. These contained C termini with leucine–rich repeats (FBXLs, e.g., SKP2 (OMIM Ref. No. 601436)), WD40 domains (FBXWs, e.g., BTRCP (OMIM Ref. No. 603482)), or no recognizable motifs (FBXOs, e.g., CCNF). By Northern blot analysis, Cenciarelli et al. (1999) found ubiquitous expression of an approximately 4.4–kb FBXL3A transcript. Immunofluorescence microscopy demonstrated nuclear localization for both wildtype FBXL3A and mutant FBXL3A lacking the F box.

[42096] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42097] Cenciarelli, C.; Chiaur, D. S.; Guardavaccaro, D.; Parks, W.; Vidal, M.; Pagano, M. : Identification of a family of human F-box proteins. Curr. Biol. 9: 1177–1179, 1999. ; and

[42098] Chiaur, D. S.; Murthy, S.; Cenciarelli, C.; Parks, W.; Loda, M.; Inghirami, G.; Demetrick, D.; Pagano, M. : Five human genes encoding F-box proteins: chromosome mapping and analysis in.

[42099] Further studies establishing the function and utilities of FBXL3A are found in John Hopkins OMIM database record ID 605653, and in cited publications numbered 40 and 416 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424) is another VGAM1172 host target gene. CECR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CECR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR1 BINDING SITE, designated SEQ

ID:18881, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42100] Another function of VGAM1172 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR1. Cortactin Binding Protein 2 (CORTBP2, Accession NM_033427) is another VGAM1172 host target gene. CORTBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORTBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORTBP2 BINDING SITE, designated SEQ ID:27250, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42101] Another function of VGAM1172 is therefore inhibition of Cortactin Binding Protein 2 (CORTBP2, Accession NM_033427). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with CORTBP2. KIAA1900 (Accession XM_055299) is another VGAM1172 host target gene. KIAA1900 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1900 BINDING SITE, designated SEQ ID:36257, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42102] Another function of VGAM1172 is therefore inhibition of KIAA1900 (Accession XM_055299). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1900. Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580) is another VGAM1172 host target gene. MKRN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MKRN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN2 BINDING SITE, designated SEQ

ID:35856, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42103] Another function of VGAM1172 is therefore inhibition of Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN2. LOC144182 (Accession NM_139136) is another VGAM1172 host target gene. LOC144182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144182 BINDING SITE, designated SEQ ID:29168, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42104] Another function of VGAM1172 is therefore inhibition of LOC144182 (Accession NM_139136). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144182. LOC151878 (Accession XM_087329) is an-

other VGAM1172 host target gene. LOC151878 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151878 BINDING SITE, designated SEQ ID:39171, to the nucleotide sequence of VGAM1172 RNA, herein designated VGAM RNA, also designated SEQ ID:3883.

[42105] Another function of VGAM1172 is therefore inhibition of LOC151878 (Accession XM_087329). Accordingly, utilities of VGAM1172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151878. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1173 (VGAM1173) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42106] VGAM1173 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1173 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[42107] VGAM1173 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cucumber Fruit Mottle Mosaic Virus. VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42108] VGAM1173 gene encodes a VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1173 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1173 precursor RNA is designated SEQ ID:1159, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1159 is located at position 5471 relative to the genome of Cucumber Fruit Mottle Mosaic Virus.

[42109] VGAM1173 precursor RNA folds onto itself, forming VGAM1173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42110] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1173 folded precursor RNA into VGAM1173 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1173 RNA is designated SEQ ID:3884, and is provided hereinbelow with reference to the sequence listing part.

[42111] VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1173 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42112] VGAM1173 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1173 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1173 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1173 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42113] The complementary binding of VGAM1173 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1173 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1173 host target RNA into VGAM1173 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42114] It is appreciated that VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1173 host target genes. The mRNA of each one of this plurality of VGAM1173 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1173 RNA, herein designated VGAM RNA, and which when bound by VGAM1173 RNA causes inhibition of translation of respective one or more VGAM1173 host target proteins.

[42115] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1173 gene, herein designated VGAM GENE, on one or more VGAM1173 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42116] It is yet further appreciated that a function of VGAM1173 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of viral infection by Cucumber Fruit Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1173 correlate with, and may be deduced from, the identity of the host target genes which VGAM1173 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42117] Nucleotide sequences of the VGAM1173 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1173 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1173 are further described hereinbelow with reference to Table 1.

[42118] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1173 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1173 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42119] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1173 gene, herein designated VGAM is inhibition of expression of VGAM1173 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1173 correlate with, and may be deduced from, the identity of the target genes which VGAM1173 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42120] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139025) is a VGAM1173 host target gene. ADAMTS13 BINDING SITE1 through ADAMTS13 BINDING SITE3 are HOST TARGET binding sites found in untrans-

lated regions of mRNA encoded by ADAMTS13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS13 BINDING SITE1 through ADAMTS13 BINDING SITE3, designated SEQ ID:29125, SEQ ID:29127 and SEQ ID:29131 respectively, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42121] A function of VGAM1173 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139025), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS13. The function of ADAMTS13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131.CCAAT/enhancer Binding Protein (C/EBP), Alpha (CEBPA, Accession NM_004364) is another VGAM1173 host target gene. CEBPA BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by CEBPA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEBPA BINDING SITE, designated SEQ ID:10573, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42122] Another function of VGAM1173 is therefore inhibition of CCAAT/enhancer Binding Protein (C/EBP), Alpha (CEBPA, Accession NM_004364). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEBPA. Heat Shock 70kDa Protein 4 (HSPA4, Accession XM_114482) is another VGAM1173 host target gene. HSPA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSPA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA4 BINDING SITE, designated SEQ ID:42977, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ

ID:3884.

[42123] Another function of VGAM1173 is therefore inhibition of Heat Shock 70kDa Protein 4 (HSPA4, Accession XM_114482). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA4. Heat Shock 60kDa Protein 1 (chaperonin) (HSPD1, Accession XM_012182) is another VGAM1173 host target gene. HSPD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPD1 BINDING SITE, designated SEQ ID:30208, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42124] Another function of VGAM1173 is therefore inhibition of Heat Shock 60kDa Protein 1 (chaperonin) (HSPD1, Accession XM_012182), a gene which is implicated in mitochondrial protein import and macromolecular assembly. may facilitate the correct folding of imported proteins. may also prevent misfolding and promote the refolding and proper assembly of unfolded polypeptides generated

under stress conditions in the mitochondrial matrix. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPD1. The function of HSPD1 has been established by previous studies. Hereditary spastic paraplegia (HSP) represents a clinically and genetically heterogeneous group of neurodegenerative disorders that are characterized by progressive spasticity and weakness of the lower limbs. Seventeen different loci had been mapped, and the corresponding genes for 5 of these had been cloned and identified. Two of the 5 gene products--paraplegin (SPG7; 602783) and spastin (SPG4; 182601)--feature AAA+ domains and are predicted to possess chaperone activity. Paraplegin is the human homolog of a yeast protease/chaperone that is involved in mitochondrial protein quality control. The HSP60 gene maps to the same region, namely 2q33.1, as does spastic paraplegia-13 (SPG13; 605280), as determined by Fontaine et al. (2000). Speculating that the mitochondrial chaperonin HSP60 or its co-chaperonin HSP10 (OMIM Ref. No. 600141), which maps to the same region, might be the site of mutation(s) causing SPG13, Hansen et al. (2002) sequenced HSP60 in 2 affected members of the

family with SPG13. They found that both were heterozygous for a G-to-A variation at position 292 of the HSP60 cDNA, resulting in the substitution of a valine at position 72 in the mature HSP60 by isoleucine (V72I). Studies in *E. coli* indicated that the V72I mutant protein is functionally incapacitated. The authors suggested that SPG4, SPG7, and SPG13 can be referred to as chaperonopathies. Azem et al. (1994) performed chemical cross-linking and electron microscopy studies on bacterial chaperonins GroEL and GroES to determine how they interact with unfolded proteins. GroEL is an oligomer of 14 identical 57.3-kD subunits, with a structure of 2 stacked heptameric rings arranged around a 2-fold axis of symmetry (Saibil et al., 1991). It appears as a hollow cylinder. In the presence of ATP, 2 GroES (see OMIM Ref. No. 600141) rings (each made of 7 identical 10.4-kD subunits) can successively bind a single GroEL core to make a functional symmetric heterodimer. Although the central core of GroEL is obstructed by the 2 GroES rings at each end, this heterodimer can stably bind and assist the refolding of the RuBisCo enzyme. While binding was thought to occur in the central cavity, these data indicate that unfolded proteins may bind and fold on the external envelope of some

chaperonins (Azem et al., 1994). Schmidt et al. (1994) suggested that the symmetric chaperonin complex is functionally significant because complete folding of a nonnative substrate protein in the presence of GroEL and GroES occurs only in the presence of ATP, and not with ADP. Chaperonin-assisted folding occurs by a catalytic cycle in which one ATP is hydrolyzed by one ring of GroEL in a quantized manner with each turnover. Todd et al. (1994) proposed a unifying model for chaperonin-facilitated protein folding based on successive rounds of binding and release, and partitioning between committed and kinetically trapped intermediates.

[42125] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42126] Fontaine, B.; Davoine, C.-S.; Durr, A.; Paternotte, C.; Feki, I.; Weissenbach, J.; Hazan, J.; Brice, A. : A new locus for autosomal dominant pure spastic paraplegia, on chromosome 2q24-q34. *Am. J. Hum. Genet.* 66: 702-707, 2000. ; and

[42127] Hansen, J. J.; Durr, A.; Cournu-Rebeix, I.; Georgopoulos, C.; Ang, D.; Nielsen, M. N.; Davoine, C.-S.; Brice, A.; Fontaine, B.; Gregersen, N.; Bross, P. : Hereditary spastic

paraplegia SPG.

[42128] Further studies establishing the function and utilities of HSPD1 are found in John Hopkins OMIM database record ID 118190, and in cited publications numbered 840–843, 10688–84 and 10689 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM_003679) is another VGAM1173 host target gene. KMO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KMO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KMO BINDING SITE, designated SEQ ID:9783, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42129] Another function of VGAM1173 is therefore inhibition of Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM_003679), a gene which may play a role in encephalic photoreception. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with KMO. The function of KMO and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM162. Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM_000901) is another VGAM1173 host target gene. NR3C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR3C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR3C2 BINDING SITE, designated SEQ ID:6599, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42130] Another function of VGAM1173 is therefore inhibition of Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM_000901), a gene which is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C2. The function of NR3C2 and

its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM186. Origin Recognition Complex, Subunit 2-like (yeast) (ORC2L, Accession NM_006190) is another VGAM1173 host target gene. ORC2L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ORC2L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ORC2L BINDING SITE, designated SEQ ID:12864, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42131] Another function of VGAM1173 is therefore inhibition of Origin Recognition Complex, Subunit 2-like (yeast) (ORC2L, Accession NM_006190), a gene which is a subunit of the origin recognition complex and may be required for initiation of DNA replication. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ORC2L. The function of ORC2L has been established by previous studies. The origin recognition complex (ORC) is a multi-

protein assemblage identified in *S. cerevisiae* that binds to the ARS (autonomously replicating sequence) consensus, a DNA motif that is an essential part of yeast origins of replication. ORC binding has also been implicated in transcriptional silencing at certain yeast loci. One component of the ORC is a 72-kD protein designated ORC2, mutations of which disrupt silencing at the HMR-E silencer and cause cell cycle arrest between late G1 and the initiation of DNA replication. Takahara et al. (1996) isolated a cDNA from a mouse embryonic stem cell library and a human placenta library whose predicted 577-amino acid protein resembles the yeast sequence. The mouse and human sequences of the ORC2L (ORC2-like) proteins are 47.9% and 46.3% similar to yeast ORC2, respectively. Northern blots showed highest levels of ORC2L expression in testes. Dhar et al. (2001) used homologous recombination to replace the third exon encoding the initiator ATG of the ORC2 gene with a neomycin phosphotransferase gene in a colon carcinoma cell line. This hypomorphic mutation decreased ORC2 protein levels by 90%. The G1 phase of the cell cycle was prolonged, but there was no effect on the utilization of either the MYC (OMIM Ref. No. 190080) or beta-globin (OMIM Ref. No. 141900) cellular origins of replication.

Cells carrying the ORC2 mutation failed to support the replication of a plasmid bearing the oriP replicator of Epstein-Barr virus (EBV), and this defect could be rescued by reintroduction of ORC2. ORC2 specifically associated with oriP in cells, most likely through its interaction with EBV nuclear antigen-1. Geminin (OMIM Ref. No. 602842), an inhibitor of the mammalian replication initiation complex, inhibited replication from oriP. Therefore, ORC and the human replication initiation apparatus is required for replication from a viral origin of replication.

[42132] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42133] Dhar, S. K.; Yoshida, K.; Machida, Y.; Khaira, P.; Chaudhuri, B.; Wohlschlegel, J. A.; Leffak, M.; Yates, J.; Dutta, A. : Replication from oriP of Epstein-Barr virus requires human ORC and is inhibited by geminin. Cell 106: 287-296, 2001. ; and

[42134] Takahara, K.; Bong, M.; Brevard, R.; Eddy, R. L.; Haley, L. L.; Sait, S. J.; Shows, T. B.; Hoffman, G. G.; Greenspan, D. S. : Mouse and human homologues of the yeast origin of replica.

[42135] Further studies establishing the function and utilities of

ORC2L are found in John Hopkins OMIM database record ID 601182, and in cited publications numbered 9505–9508 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PACE (Accession NM_002569) is another VGAM1173 host target gene. PACE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE BINDING SITE, designated SEQ ID:8428, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42136] Another function of VGAM1173 is therefore inhibition of PACE (Accession NM_002569), a gene which processes pro-parathyroid hormone, pro-transforming growth factor beta. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE. The function of PACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM151. Protocadherin 11 X-linked (PCDH11X, Acces-

sion NM_032968) is another VGAM1173 host target gene. PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11X, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2, designated SEQ ID:26796 and SEQ ID:26811 respectively, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42137] Another function of VGAM1173 is therefore inhibition of Protocadherin 11 X-linked (PCDH11X, Accession NM_032968), a gene which is thought to play a fundamental role in cell-cell recognition essential for the segmental development and function of the central nervous system. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11X. The function of PCDH11X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433. Protein Phosphatase 1, Regulatory (inhibitor)

Subunit 11 (PPP1R11, Accession NM_021959) is another VGAM1173 host target gene. PPP1R11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R11 BINDING SITE, designated SEQ ID:22485, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42138] Another function of VGAM1173 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 11 (PPP1R11, Accession NM_021959), a gene which inhibits rabbit muscle protein phosphatase-1 in vitro . Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R11. The function of PPP1R11 has been established by previous studies. Using a cDNA selection technique to identify genes in the hemochromatosis (OMIM Ref. No. 235200) gene region on 6p21.3, El Kahloun et al. (1993) cloned PPP1R11, which they called HCGV (hemochromatosis candidate gene V). By screening cDNA libraries and using PCR techniques, Giffon et al.

(1996) obtained a full-length cDNA encoding PPP1R11. The predicted 126-amino acid PPP1R11 protein contains 8 potential phosphorylation sites and a C-terminal PEST pattern that is characteristic of proteins with short half-lives. PPP1R11 shares 89.7% amino acid identity with its mouse homolog, Tctex5. Northern blot analysis detected a 1.8-kb PPP1R11 transcript in all fetal and adult tissues tested. The PPP1R11 gene appeared to be widely preserved throughout animal evolution, and Giffon et al. (1996) detected fragments on the DNAs of primates, rat, dog, cow, and rabbit. By screening sequence databases, Lepourcelet et al. (1996) identified a cDNA clone that suggested the existence of at least 1 spliced isoform of PPP1R11. Using a yeast 2-hybrid screen to identify putative protein phosphatase-1 (PP1; OMIM Ref. No. 176875)-binding proteins, Zhang et al. (1998) obtained a cDNA encoding PPP1R11, which they called inhibitor-3. They reported that PPP1R11 is hydrophilic, heat stable, and behaves anomalously on SDS-PAGE, with an apparent molecular mass of 23 kD compared with its calculated molecular mass of 14 kD, and on gel filtration, with a relative molecular weight of 55,000. Zhang et al. (1998) showed that PPP1R11 is a specific inhibitor of PP1 with a

differential sensitivity toward the metal-independent and metal-dependent forms of PP1. They hypothesized that the PP1-binding ability of PPP1R11 is due at least in part to the possession of a VxW motif. PPP1R11 is well conserved in evolution, with related genes in *S. cerevisiae*, *S. pombe*, and *C. elegans*.

[42139] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42140] Lepourcelet, M.; Andrieux, N.; Giffon, T.; Pichon, L.; Hampe, A.; Galibert, F.; Mosser, J. : Systematic sequencing of the human HLA-A/HLA-F region: establishment of a cosmid contig and identification of a new gene cluster within 37 kb of sequence. *Genomics* 37: 316-326, 1996. ; and

[42141] Zhang, J.; Zhang, L.; Zhao, S.; Lee, E. Y. C. : Identification and characterization of the human HCG V gene product as a novel inhibitor of protein phosphatase-1. *Biochemistry* 37: 16728.

[42142] Further studies establishing the function and utilities of PPP1R11 are found in John Hopkins OMIM database record ID 606670, and in cited publications numbered 910 and 9568-6456 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Ubiquitin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087) is another VGAM1173 host target gene. UBE2G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G2 BINDING SITE, designated SEQ ID:32378, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42143] Another function of VGAM1173 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G2. The function of UBE2G2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164. Angiotensin II Receptor-like 2 (AGTRL2, Acces-

sion NM_005162) is another VGAM1173 host target gene. AGTRL2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AGTRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGTRL2 BINDING SITE, designated SEQ ID:11648, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42144] Another function of VGAM1173 is therefore inhibition of Angiotensin II Receptor-like 2 (AGTRL2, Accession NM_005162). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTRL2. ARP3BETA (Accession NM_020445) is another VGAM1173 host target gene. ARP3BETA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARP3BETA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARP3BETA BINDING SITE, designated SEQ ID:21687, to the nucleotide sequence of VGAM1173

RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42145] Another function of VGAM1173 is therefore inhibition of ARP3BETA (Accession NM_020445). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARP3BETA. DCOHM (Accession NM_032151) is another VGAM1173 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25852, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42146] Another function of VGAM1173 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. DKFZp566H0824 (Accession NM_017535) is another VGAM1173 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the

5` untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated SEQ ID:18981, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42147] Another function of VGAM1173 is therefore inhibition of DKFZp566H0824 (Accession NM_017535). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566H0824. EFA6R (Accession NM_015310) is another VGAM1173 host target gene. EFA6R BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EFA6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFA6R BINDING SITE, designated SEQ ID:17628, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42148] Another function of VGAM1173 is therefore inhibition of

EFA6R (Accession NM_015310). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFA6R. Epiregulin (EREG, Accession NM_001432) is another VGAM1173 host target gene. EREG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EREG BINDING SITE, designated SEQ ID:7158, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42149] Another function of VGAM1173 is therefore inhibition of Epiregulin (EREG, Accession NM_001432). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EREG. FLJ10656 (Accession NM_018170) is another VGAM1173 host target gene. FLJ10656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10656 BINDING SITE, designated SEQ ID:19992, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42150] Another function of VGAM1173 is therefore inhibition of FLJ10656 (Accession NM_018170). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10656. FLJ10891 (Accession NM_018260) is another VGAM1173 host target gene. FLJ10891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10891 BINDING SITE, designated SEQ ID:20227, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42151] Another function of VGAM1173 is therefore inhibition of FLJ10891 (Accession NM_018260). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10891. FLJ21106 (Accession NM_025097) is another

VGAM1173 host target gene. FLJ21106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21106 BINDING SITE, designated SEQ ID:24739, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42152] Another function of VGAM1173 is therefore inhibition of FLJ21106 (Accession NM_025097). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21106. FLJ23511 (Accession NM_032239) is another VGAM1173 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25970, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42153] Another function of VGAM1173 is therefore inhibition of FLJ23511 (Accession NM_032239). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. KIAA0152 (Accession NM_014730) is another VGAM1173 host target gene. KIAA0152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE, designated SEQ ID:16343, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42154] Another function of VGAM1173 is therefore inhibition of KIAA0152 (Accession NM_014730). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0152. KIAA0940 (Accession NM_014912) is another VGAM1173 host target gene. KIAA0940 BINDING SITE1 and KIAA0940 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0940, corresponding to HOST TARGET binding sites

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0940 BINDING SITE1 and KIAA0940 BINDING SITE2, designated SEQ ID:17150 and SEQ ID:17151 respectively, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42155] Another function of VGAM1173 is therefore inhibition of KIAA0940 (Accession NM_014912). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0940. Mitochondrial Ribosomal Protein S10 (MRPS10, Accession NM_018141) is another VGAM1173 host target gene. MRPS10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS10 BINDING SITE, designated SEQ ID:19941, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42156] Another function of VGAM1173 is therefore inhibition of

Mitochondrial Ribosomal Protein S10 (MRPS10, Accession NM_018141). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS10. SDS3 (Accession XM_045014) is another VGAM1173 host target gene. SDS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDS3 BINDING SITE, designated SEQ ID:34322, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42157] Another function of VGAM1173 is therefore inhibition of SDS3 (Accession XM_045014). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDS3. Serine/threonine Kinase 3 (STE20 homolog, yeast) (STK3, Accession XM_057232) is another VGAM1173 host target gene. STK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of STK3 BINDING SITE, designated SEQ ID:36495, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42158] Another function of VGAM1173 is therefore inhibition of Serine/threonine Kinase 3 (STE20 homolog, yeast) (STK3, Accession XM_057232). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK3. TUCAN (Accession NM_014959) is another VGAM1173 host target gene. TUCAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUCAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUCAN BINDING SITE, designated SEQ ID:17322, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42159] Another function of VGAM1173 is therefore inhibition of TUCAN (Accession NM_014959). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUCAN.

ZNF340 (Accession XM_097701) is another VGAM1173 host target gene. ZNF340 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF340 BINDING SITE, designated SEQ ID:41036, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42160] Another function of VGAM1173 is therefore inhibition of ZNF340 (Accession XM_097701). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF340. LOC143785 (Accession XM_084635) is another VGAM1173 host target gene. LOC143785 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143785, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143785 BINDING SITE, designated SEQ ID:37633, to the nucleotide sequence of VGAM1173 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3884.

[42161] Another function of VGAM1173 is therefore inhibition of LOC143785 (Accession XM_084635). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143785. LOC144453 (Accession XM_084869) is another VGAM1173 host target gene. LOC144453 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144453 BINDING SITE, designated SEQ ID:37749, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42162] Another function of VGAM1173 is therefore inhibition of LOC144453 (Accession XM_084869). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144453. LOC148824 (Accession XM_097527) is another VGAM1173 host target gene. LOC148824 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148824, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148824 BINDING SITE, designated SEQ ID:40910, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42163] Another function of VGAM1173 is therefore inhibition of LOC148824 (Accession XM_097527). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148824. LOC200471 (Accession XM_117234) is another VGAM1173 host target gene. LOC200471 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200471 BINDING SITE, designated SEQ ID:43305, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42164] Another function of VGAM1173 is therefore inhibition of LOC200471 (Accession XM_117234). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC200471. LOC201696 (Accession XM_032269) is another VGAM1173 host target gene. LOC201696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201696 BINDING SITE, designated SEQ ID:31628, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42165] Another function of VGAM1173 is therefore inhibition of LOC201696 (Accession XM_032269). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201696. LOC257465 (Accession XM_088384) is another VGAM1173 host target gene. LOC257465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257465 BINDING SITE, designated SEQ ID:39668, to

the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42166] Another function of VGAM1173 is therefore inhibition of LOC257465 (Accession XM_088384). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257465. LOC91408 (Accession XM_038290) is another VGAM1173 host target gene. LOC91408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91408 BINDING SITE, designated SEQ ID:32794, to the nucleotide sequence of VGAM1173 RNA, herein designated VGAM RNA, also designated SEQ ID:3884.

[42167] Another function of VGAM1173 is therefore inhibition of LOC91408 (Accession XM_038290). Accordingly, utilities of VGAM1173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91408. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1174 (VGAM1174) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42168] VGAM1174 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1174 was detected is described hereinabove with reference to Figs. 1–8.

[42169] VGAM1174 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rift Valley Fever Virus. VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42170] VGAM1174 gene encodes a VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1174 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1174 precursor RNA is designated SEQ ID:1160, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1160 is located at position 4915 relative to the genome of Rift Valley Fever Virus.

[42171] VGAM1174 precursor RNA folds onto itself, forming VGAM1174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42172] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1174 folded precursor RNA into VGAM1174 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1174 RNA is designated SEQ ID:3885, and is provided hereinbelow with reference to the sequence listing part.

[42173] VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1174 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1174 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42174] VGAM1174 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1174 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1174 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42175] The complementary binding of VGAM1174 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1174 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1174 host target RNA into VGAM1174 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42176] It is appreciated that VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1174 host target genes. The mRNA of each one of this plurality of VGAM1174 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1174 RNA, herein designated VGAM RNA, and which when bound by VGAM1174 RNA causes inhibition of translation of respective one or more VGAM1174 host target proteins.

[42177] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1174 gene, herein designated VGAM GENE, on one or more VGAM1174 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42178] It is yet further appreciated that a function of VGAM1174 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1174 include diagnosis, prevention and treatment of viral infection by Rift Valley Fever Virus. Specific functions, and accordingly utilities, of VGAM1174 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1174 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42179] Nucleotide sequences of the VGAM1174 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1174 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1174 are further described hereinbelow with reference to Table 1.

[42180] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1174 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1174 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42181] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1174 gene, herein designated VGAM is inhibition of expression of VGAM1174 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1174 correlate with, and may be deduced from, the identity of the target genes which VGAM1174

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42182] LHPP (Accession NM_022126) is a VGAM1174 host target gene. LHPP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LHPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHPP BINDING SITE, designated SEQ ID:22674, to the nucleotide sequence of VGAM1174 RNA, herein designated VGAM RNA, also designated SEQ ID:3885.

[42183] A function of VGAM1174 is therefore inhibition of LHPP (Accession NM_022126). Accordingly, utilities of VGAM1174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHPP. LOC151584 (Accession XM_098089) is another VGAM1174 host target gene. LOC151584 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151584 BINDING SITE, designated SEQ ID:41376, to

the nucleotide sequence of VGAM1174 RNA, herein designated VGAM RNA, also designated SEQ ID:3885.

[42184] Another function of VGAM1174 is therefore inhibition of LOC151584 (Accession XM_098089). Accordingly, utilities of VGAM1174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151584. LOC201799 (Accession XM_114380) is another VGAM1174 host target gene. LOC201799 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201799, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201799 BINDING SITE, designated SEQ ID:42914, to the nucleotide sequence of VGAM1174 RNA, herein designated VGAM RNA, also designated SEQ ID:3885.

[42185] Another function of VGAM1174 is therefore inhibition of LOC201799 (Accession XM_114380). Accordingly, utilities of VGAM1174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201799. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1175 (VGAM1175) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42186] VGAM1175 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1175 was detected is described hereinabove with reference to Figs. 1–8.

[42187] VGAM1175 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rift Valley Fever Virus. VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42188] VGAM1175 gene encodes a VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1175 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1175 precursor RNA is designated SEQ ID:1161, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1161 is located at position 5974 relative to the genome of Rift Valley Fever Virus.

[42189] VGAM1175 precursor RNA folds onto itself, forming VGAM1175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42190] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1175 folded precursor RNA into VGAM1175 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1175 RNA is designated SEQ ID:3886, and is provided hereinbelow with reference to the sequence listing part.

[42191] VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1175 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1175 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42192] VGAM1175 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1175 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1175 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42193] The complementary binding of VGAM1175 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1175 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1175 host target RNA into VGAM1175 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42194] It is appreciated that VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1175 host target genes. The mRNA of each one of this plurality of VGAM1175 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1175 RNA, herein designated VGAM RNA, and which when bound by VGAM1175 RNA causes inhibition of translation of respective one or more VGAM1175 host target proteins.

[42195] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1175 gene, herein designated VGAM GENE, on one or more VGAM1175 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42196] It is yet further appreciated that a function of VGAM1175 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of viral infection by Rift Valley Fever Virus. Specific functions, and accordingly utilities, of VGAM1175 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1175 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42197] Nucleotide sequences of the VGAM1175 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1175 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1175 are further described hereinbelow with reference to Table 1.

[42198] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1175 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1175 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42199] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1175 gene, herein designated VGAM is inhibition of expression of VGAM1175 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1175 correlate with, and may be deduced from, the identity of the target genes which VGAM1175

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42200] Lunatic Fringe Homolog (Drosophila) (LFNG, Accession XM_166539) is a VGAM1175 host target gene. LFNG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFNG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFNG BINDING SITE, designated SEQ ID:44510, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42201] A function of VGAM1175 is therefore inhibition of Lunatic Fringe Homolog (Drosophila) (LFNG, Accession XM_166539). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFNG. MGC3178 (Accession NM_030810) is another VGAM1175 host target gene. MGC3178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of MGC3178 BINDING SITE, designated SEQ ID:25132, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42202] Another function of VGAM1175 is therefore inhibition of MGC3178 (Accession NM_030810). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3178. Transducer of ERBB2, 2 (TOB2, Accession XM_170995) is another VGAM1175 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45772, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42203] Another function of VGAM1175 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM_170995). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC145501 (Accession

XM_085157) is another VGAM1175 host target gene.

LOC145501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145501 BINDING SITE, designated SEQ ID:37883, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42204] Another function of VGAM1175 is therefore inhibition of LOC145501 (Accession XM_085157). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145501. LOC147671 (Accession XM_085844) is another VGAM1175 host target gene. LOC147671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147671 BINDING SITE, designated SEQ ID:38379, to the nucleotide sequence of VGAM1175 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3886.

[42205] Another function of VGAM1175 is therefore inhibition of LOC147671 (Accession XM_085844). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147671. LOC157273 (Accession XM_098743) is another VGAM1175 host target gene. LOC157273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157273 BINDING SITE, designated SEQ ID:41788, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42206] Another function of VGAM1175 is therefore inhibition of LOC157273 (Accession XM_098743). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157273. LOC91380 (Accession XM_038134) is another VGAM1175 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91380, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32759, to the nucleotide sequence of VGAM1175 RNA, herein designated VGAM RNA, also designated SEQ ID:3886.

[42207] Another function of VGAM1175 is therefore inhibition of LOC91380 (Accession XM_038134). Accordingly, utilities of VGAM1175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1176 (VGAM1176) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42208] VGAM1176 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1176 was detected is described hereinabove with reference to Figs. 1-8.

[42209] VGAM1176 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rift Valley Fever Virus.

VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42210] VGAM1176 gene encodes a VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1176 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1176 precursor RNA is designated SEQ ID:1162, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1162 is located at position 2112 relative to the genome of Rift Valley Fever Virus.

[42211] VGAM1176 precursor RNA folds onto itself, forming VGAM1176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42212] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1176 folded precursor RNA into VGAM1176 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1176 RNA is designated SEQ ID:3887, and is provided hereinbelow with reference to the sequence listing part.

[42213] VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1176 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42214] VGAM1176 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1176 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1176 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42215] The complementary binding of VGAM1176 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1176 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1176 host target RNA into VGAM1176 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42216] It is appreciated that VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1176 host target genes. The mRNA of each one of this plurality of VGAM1176 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1176 RNA, herein designated VGAM RNA, and which when bound by VGAM1176 RNA causes inhibition of translation of respective one or more VGAM1176 host target proteins.

[42217] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1176 gene, herein designated VGAM GENE, on one or more VGAM1176 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42218] It is yet further appreciated that a function of VGAM1176 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of viral infection by Rift Valley Fever Virus. Specific functions, and accordingly utilities, of VGAM1176 correlate with, and may be deduced from, the identity of the host target genes which VGAM1176 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42219] Nucleotide sequences of the VGAM1176 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1176 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1176 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1176 are further described hereinbelow with reference to Table 1.

[42220] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1176 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1176 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42221] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1176 gene, herein designated VGAM is inhibition of expression of VGAM1176 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1176 correlate with, and may be deduced from, the identity of the target genes which VGAM1176 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42222] Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282) is a VGAM1176 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ

ID:6955, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42223] A function of VGAM1176 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282), a gene which links clathrin to receptors in coated vesicles. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093) is another VGAM1176 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11552, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ

ID:3887.

[42224] Another function of VGAM1176 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Collagen, Type IV, Alpha 6 (COL4A6, Accession NM_033641) is another VGAM1176 host target gene. COL4A6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by COL4A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A6 BINDING SITE, designated SEQ ID:27360, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42225] Another function of VGAM1176 is therefore inhibition of Collagen, Type IV, Alpha 6 (COL4A6, Accession

NM_033641). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A6. EphB1 (EPHB1, Accession NM_004441) is another VGAM1176 host target gene. EPHB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB1 BINDING SITE, designated SEQ ID:10728, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42226] Another function of VGAM1176 is therefore inhibition of EphB1 (EPHB1, Accession NM_004441), a gene which receptor for members of the ephrin-b family. binds to ephrin-b1, -b2 and -b3. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB1. The function of EPHB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1000. Guanine Nucleotide Binding Protein (G pro-

tein), Beta Polypeptide 3 (GNB3, Accession NM_002075) is another VGAM1176 host target gene. GNB3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GNB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB3 BINDING SITE, designated SEQ ID:7854, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42227] Another function of VGAM1176 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 3 (GNB3, Accession NM_002075), a gene which transduces signals from G protein-coupled receptors to intracellular effectors. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB3. The function of GNB3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Glypican 1 (GPC1, Accession NM_002081) is another VGAM1176 host target gene. GPC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by GPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC1 BINDING SITE, designated SEQ ID:7871, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42228] Another function of VGAM1176 is therefore inhibition of Glypican 1 (GPC1, Accession NM_002081), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC1. The function of GPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275) is another VGAM1176 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BIND-

ING SITE, designated SEQ ID:14600, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42229] Another function of VGAM1176 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM263. Matrix Metalloproteinase 19 (MMP19, Accession NM_022791) is another VGAM1176 host target gene. MMP19 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MMP19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE, designated SEQ ID:23080, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42230] Another function of VGAM1176 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_022791). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. Nuclear RNA Export Factor 2 (NXF2, Accession NM_022053) is another VGAM1176 host target gene. NXF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NXF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXF2 BINDING SITE, designated SEQ ID:22591, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42231] Another function of VGAM1176 is therefore inhibition of Nuclear RNA Export Factor 2 (NXF2, Accession NM_022053), a gene which is involved in the export of mrna from the nucleus to the cytoplasm. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXF2. The function of NXF2 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM595. Oligophrenin 1 (OPHN1, Accession NM_002547) is another VGAM1176 host target gene.

OPHN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8406, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42232] Another function of VGAM1176 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM_002547). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPHN1. Podocalyxin-like (PODXL, Accession NM_005397) is another VGAM1176 host target gene. PODXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PODXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PODXL BINDING SITE, designated SEQ ID:11873, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42233] Another function of VGAM1176 is therefore inhibition of Podocalyxin-like (PODXL, Accession NM_005397), a gene which is an antiadhesin. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PODXL. The function of PODXL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession NM_002933) is another VGAM1176 host target gene. RNASE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNASE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNASE1 BINDING SITE, designated SEQ ID:8837, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42234] Another function of VGAM1176 is therefore inhibition of Ribonuclease, RNase A Family, 1 (pancreatic) (RNASE1, Accession NM_002933), a gene which is a Pancreatic ribonuclease; a pyrimidine-specific endonuclease that generates 2',3'-cyclic phosphate products. Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNASE1. The function of RNASE1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210. Caspase Recruitment Domain Family, Member 14 (CARD14, Accession NM_052819) is another VGAM1176 host target gene. CARD14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CARD14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD14 BINDING SITE, designated SEQ ID:27407, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42235] Another function of VGAM1176 is therefore inhibition of Caspase Recruitment Domain Family, Member 14

(CARD14, Accession NM_052819). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD14. Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273) is another VGAM1176 host target gene. CHST3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST3 BINDING SITE, designated SEQ ID:10482, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42236] Another function of VGAM1176 is therefore inhibition of Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST3. DKFZP586B2420 (Accession XM_059482) is another VGAM1176 host target gene. DKFZP586B2420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586B2420,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586B2420 BINDING SITE, designated SEQ ID:37010, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42237] Another function of VGAM1176 is therefore inhibition of DKFZP586B2420 (Accession XM_059482). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586B2420. DKFZp586I021 (Accession NM_032271) is another VGAM1176 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26023, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42238] Another function of VGAM1176 is therefore inhibition of

DKFZp586I021 (Accession NM_032271). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. DRIL2 (Accession NM_006465) is another VGAM1176 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13186, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42239] Another function of VGAM1176 is therefore inhibition of DRIL2 (Accession NM_006465). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. FLB6421 (Accession NM_020119) is another VGAM1176 host target gene. FLB6421 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLB6421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLB6421 BINDING SITE, designated SEQ ID:21301, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42240] Another function of VGAM1176 is therefore inhibition of FLB6421 (Accession NM_020119). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLB6421. FLJ10521 (Accession NM_018125) is another VGAM1176 host target gene. FLJ10521 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10521, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10521 BINDING SITE, designated SEQ ID:19910, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42241] Another function of VGAM1176 is therefore inhibition of FLJ10521 (Accession NM_018125). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10521. FLJ10620 (Accession NM_018157) is another

VGAM1176 host target gene. FLJ10620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10620 BINDING SITE, designated SEQ ID:19975, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42242] Another function of VGAM1176 is therefore inhibition of FLJ10620 (Accession NM_018157). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10620. FLJ10751 (Accession NM_018205) is another VGAM1176 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20090 and SEQ ID:20189 respectively, to the nucleotide sequence of

VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42243] Another function of VGAM1176 is therefore inhibition of FLJ10751 (Accession NM_018205). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. FLJ12547 (Accession NM_024992) is another VGAM1176 host target gene. FLJ12547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12547 BINDING SITE, designated SEQ ID:24547, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42244] Another function of VGAM1176 is therefore inhibition of FLJ12547 (Accession NM_024992). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12547. FLJ31709 (Accession NM_144636) is another VGAM1176 host target gene. FLJ31709 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ31709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31709 BINDING SITE, designated SEQ ID:29459, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42245] Another function of VGAM1176 is therefore inhibition of FLJ31709 (Accession NM_144636). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31709. Hypermethylated In Cancer 2 (HIC2, Accession XM_036937) is another VGAM1176 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32533, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42246] Another function of VGAM1176 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession

XM_036937). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. KIAA0317 (Accession NM_014821) is another VGAM1176 host target gene.

KIAA0317 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0317 BINDING SITE, designated SEQ ID:16794, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42247] Another function of VGAM1176 is therefore inhibition of KIAA0317 (Accession NM_014821). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0317. KIAA0417 (Accession XM_048898) is another VGAM1176 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0417 BINDING SITE, designated SEQ ID:35292, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42248] Another function of VGAM1176 is therefore inhibition of KIAA0417 (Accession XM_048898). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA0574 (Accession XM_045076) is another VGAM1176 host target gene. KIAA0574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0574 BINDING SITE, designated SEQ ID:34344, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42249] Another function of VGAM1176 is therefore inhibition of KIAA0574 (Accession XM_045076). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0574. KIAA0939 (Accession XM_030524) is another

VGAM1176 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31066, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42250] Another function of VGAM1176 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA1211 (Accession XM_044178) is another VGAM1176 host target gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1211 BINDING SITE, designated SEQ ID:34166, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42251] Another function of VGAM1176 is therefore inhibition of KIAA1211 (Accession XM_044178). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. KIAA1580 (Accession XM_045271) is another VGAM1176 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34407, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42252] Another function of VGAM1176 is therefore inhibition of KIAA1580 (Accession XM_045271). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1879 (Accession XM_056635) is another VGAM1176 host target gene. KIAA1879 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1879, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1879 BINDING SITE, designated SEQ ID:36415, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42253] Another function of VGAM1176 is therefore inhibition of KIAA1879 (Accession XM_056635). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1879. LanC Lantibiotic Synthetase Component C-like 2 (bacterial) (LANCL2, Accession NM_018697) is another VGAM1176 host target gene. LANCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANCL2 BINDING SITE, designated SEQ ID:20776, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42254] Another function of VGAM1176 is therefore inhibition of LanC Lantibiotic Synthetase Component C-like 2 (bacterial) (LANCL2, Accession NM_018697). Accordingly,

utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANCL2. MAC30 (Accession XM_031536) is another VGAM1176 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MAC30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ ID:31405, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42255] Another function of VGAM1176 is therefore inhibition of MAC30 (Accession XM_031536). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP3K3, Accession NM_002401) is another VGAM1176 host target gene. MAP3K3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAP3K3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MAP3K3 BINDING SITE, designated SEQ ID:8224, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42256] Another function of VGAM1176 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 3 (MAP3K3, Accession NM_002401). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K3. MGC4368 (Accession NM_024510) is another VGAM1176 host target gene. MGC4368 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4368 BINDING SITE, designated SEQ ID:23699, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42257] Another function of VGAM1176 is therefore inhibition of MGC4368 (Accession NM_024510). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC4368. NIFU (Accession XM_041081) is another VGAM1176 host target gene. NIFU BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NIFU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIFU BINDING SITE, designated SEQ ID:33437, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42258] Another function of VGAM1176 is therefore inhibition of NIFU (Accession XM_041081). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIFU. RALGPS1A (Accession NM_014636) is another VGAM1176 host target gene. RALGPS1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RALGPS1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALGPS1A BINDING SITE, designated SEQ ID:16017, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA,

also designated SEQ ID:3887.

[42259] Another function of VGAM1176 is therefore inhibition of RALGPS1A (Accession NM_014636). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALGPS1A. TED (Accession NM_015686) is another VGAM1176 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17916, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42260] Another function of VGAM1176 is therefore inhibition of TED (Accession NM_015686). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. LOC115129 (Accession XM_055292) is another VGAM1176 host target gene. LOC115129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115129, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36254, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42261] Another function of VGAM1176 is therefore inhibition of LOC115129 (Accession XM_055292). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. LOC124977 (Accession XM_071942) is another VGAM1176 host target gene. LOC124977 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124977 BINDING SITE, designated SEQ ID:37448, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42262] Another function of VGAM1176 is therefore inhibition of LOC124977 (Accession XM_071942). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC124977. LOC138399 (Accession XM_059971) is another VGAM1176 host target gene. LOC138399 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138399 BINDING SITE, designated SEQ ID:37132, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42263] Another function of VGAM1176 is therefore inhibition of LOC138399 (Accession XM_059971). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138399. LOC142941 (Accession XM_096363) is another VGAM1176 host target gene. LOC142941 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC142941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142941 BINDING SITE, designated SEQ ID:40323, to

the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42264] Another function of VGAM1176 is therefore inhibition of LOC142941 (Accession XM_096363). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142941. LOC144481 (Accession XM_096611) is another VGAM1176 host target gene. LOC144481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144481 BINDING SITE, designated SEQ ID:40420, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42265] Another function of VGAM1176 is therefore inhibition of LOC144481 (Accession XM_096611). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144481. LOC146138 (Accession XM_096938) is another VGAM1176 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40657, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42266] Another function of VGAM1176 is therefore inhibition of LOC146138 (Accession XM_096938). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC146333 (Accession XM_091306) is another VGAM1176 host target gene. LOC146333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146333 BINDING SITE, designated SEQ ID:40045, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42267] Another function of VGAM1176 is therefore inhibition of LOC146333 (Accession XM_091306). Accordingly, utilities

of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146333. LOC149175 (Accession XM_086445) is another VGAM1176 host target gene. LOC149175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149175 BINDING SITE, designated SEQ ID:38663, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42268] Another function of VGAM1176 is therefore inhibition of LOC149175 (Accession XM_086445). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149175. LOC153883 (Accession XM_087798) is another VGAM1176 host target gene. LOC153883 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153883 BINDING SITE, designated SEQ ID:39432, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42269] Another function of VGAM1176 is therefore inhibition of LOC153883 (Accession XM_087798). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153883. LOC157931 (Accession XM_098845) is another VGAM1176 host target gene. LOC157931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157931 BINDING SITE, designated SEQ ID:41905, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42270] Another function of VGAM1176 is therefore inhibition of LOC157931 (Accession XM_098845). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157931. LOC196759 (Accession XM_113601) is another VGAM1176 host target gene. LOC196759 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196759 BINDING SITE, designated SEQ ID:42296, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42271] Another function of VGAM1176 is therefore inhibition of LOC196759 (Accession XM_113601). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196759. LOC199864 (Accession XM_117146) is another VGAM1176 host target gene. LOC199864 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199864, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199864 BINDING SITE, designated SEQ ID:43252, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42272] Another function of VGAM1176 is therefore inhibition of

LOC199864 (Accession XM_117146). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199864. LOC200734 (Accession XM_114286) is another VGAM1176 host target gene. LOC200734 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200734, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200734 BINDING SITE, designated SEQ ID:42842, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42273] Another function of VGAM1176 is therefore inhibition of LOC200734 (Accession XM_114286). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200734. LOC202934 (Accession XM_117486) is another VGAM1176 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43454, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42274] Another function of VGAM1176 is therefore inhibition of LOC202934 (Accession XM_117486). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. LOC220776 (Accession XM_043388) is another VGAM1176 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33937, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42275] Another function of VGAM1176 is therefore inhibition of LOC220776 (Accession XM_043388). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC253868 (Accession XM_170975) is an-

other VGAM1176 host target gene. LOC253868 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253868 BINDING SITE, designated SEQ ID:45749, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42276] Another function of VGAM1176 is therefore inhibition of LOC253868 (Accession XM_170975). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253868. LOC254045 (Accession XM_172882) is another VGAM1176 host target gene. LOC254045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254045 BINDING SITE, designated SEQ ID:46162, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42277] Another function of VGAM1176 is therefore inhibition of LOC254045 (Accession XM_172882). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254045. LOC255465 (Accession XM_173206) is another VGAM1176 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46448, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42278] Another function of VGAM1176 is therefore inhibition of LOC255465 (Accession XM_173206). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. LOC91351 (Accession XM_037817) is another VGAM1176 host target gene. LOC91351 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91351, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91351 BINDING SITE, designated SEQ ID:32699, to the nucleotide sequence of VGAM1176 RNA, herein designated VGAM RNA, also designated SEQ ID:3887.

[42279] Another function of VGAM1176 is therefore inhibition of LOC91351 (Accession XM_037817). Accordingly, utilities of VGAM1176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91351. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1177 (VGAM1177) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42280] VGAM1177 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1177 was detected is described hereinabove with reference to Figs. 1-8.

[42281] VGAM1177 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Odontoglossum Ringspot Virus. VGAM1177 host target gene, herein des-

ignated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42282] VGAM1177 gene encodes a VGAM1177 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1177 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1177 precursor RNA is designated SEQ ID:1163, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1163 is located at position 4157 relative to the genome of Odontoglossum Ringspot Virus.

[42283] VGAM1177 precursor RNA folds onto itself, forming VGAM1177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42284] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1177 folded precursor RNA into VGAM1177

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1177 RNA is designated SEQ ID:3888, and is provided hereinbelow with reference to the sequence listing part.

[42285] VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1177 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42286] VGAM1177 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1177 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1177 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42287] The complementary binding of VGAM1177 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1177 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1177 host target RNA into VGAM1177 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[42288] It is appreciated that VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1177 host target genes. The mRNA of each one of this plurality of VGAM1177 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1177 RNA, herein designated VGAM RNA, and which when bound by VGAM1177 RNA causes inhibition of translation of respective one or more VGAM1177 host target proteins.

[42289] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1177 gene, herein designated VGAM GENE, on one or more VGAM1177 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42290] It is yet further appreciated that a function of VGAM1177 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1177 include diagnosis, prevention and treatment of viral infection by Odontoglossum Ringspot Virus. Specific functions, and accordingly utilities, of VGAM1177 correlate with, and may be deduced from, the identity of the host target genes which VGAM1177 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42291] Nucleotide sequences of the VGAM1177 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1177 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1177 are further described hereinbelow with reference to Table 1.

[42292] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1177 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1177 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42293] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1177 gene, herein designated VGAM is inhibition of expression of VGAM1177 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1177 correlate with, and may be deduced from, the identity of the target genes which VGAM1177 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42294] Moesin (MSN, Accession XM_013042) is a VGAM1177 host target gene. MSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSN BINDING SITE, designated SEQ ID:30226, to the nucleotide sequence of VGAM1177 RNA, herein designated VGAM RNA, also designated SEQ

ID:3888.

[42295] A function of VGAM1177 is therefore inhibition of Moesin (MSN, Accession XM_013042), a gene which may have a role linking the cytoskeleton to the plasma membrane. Accordingly, utilities of VGAM1177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSN. The function of MSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM248. RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM_134422) is another VGAM1177 host target gene. RAD52 BINDING SITE1 through RAD52 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD52, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE1 through RAD52 BINDING SITE3, designated SEQ ID:28642, SEQ ID:28652 and SEQ ID:28661 respectively, to the nucleotide sequence of VGAM1177 RNA, herein designated VGAM RNA, also designated SEQ ID:3888.

[42296] Another function of VGAM1177 is therefore inhibition of

RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM_134422). Accordingly, utilities of VGAM1177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. LOC136288 (Accession XM_059832) is another VGAM1178 host target gene. LOC136288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC136288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC136288 BINDING SITE, designated SEQ ID:37098, to the nucleotide sequence of VGAM1178 RNA, herein designated VGAM RNA, also designated SEQ ID:3889.

[42297] Another function of VGAM1178 is therefore inhibition of LOC136288 (Accession XM_059832). Accordingly, utilities of VGAM1178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC136288. LOC51333 (Accession NM_016643) is another VGAM1178 host target gene. LOC51333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51333, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51333 BINDING SITE, designated SEQ ID:18749, to the nucleotide sequence of VGAM1178 RNA, herein designated VGAM RNA, also designated SEQ ID:3889.

[42298] Another function of VGAM1178 is therefore inhibition of LOC51333 (Accession NM_016643). Accordingly, utilities of VGAM1178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1179 (VGAM1179) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42299] VGAM1179 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1179 was detected is described hereinabove with reference to Figs. 1-8.

[42300] VGAM1179 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Odontoglossum Ringspot Virus. VGAM1179 host target gene, herein des-

ignated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42301] VGAM1179 gene encodes a VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1179 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1179 precursor RNA is designated SEQ ID:1165, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1165 is located at position 5650 relative to the genome of Odontoglossum Ringspot Virus.

[42302] VGAM1179 precursor RNA folds onto itself, forming VGAM1179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42303] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1179 folded precursor RNA into VGAM1179

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1179 RNA is designated SEQ ID:3890, and is provided hereinbelow with reference to the sequence listing part.

[42304] VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1179 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42305] VGAM1179 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1179 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1179 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42306] The complementary binding of VGAM1179 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1179 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1179 host target RNA into VGAM1179 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[42307] It is appreciated that VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1179 host target genes. The mRNA of each one of this plurality of VGAM1179 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1179 RNA, herein designated VGAM RNA, and which when bound by VGAM1179 RNA causes inhibition of translation of respective one or more VGAM1179 host target proteins.

[42308] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1179 gene, herein designated VGAM GENE, on one or more VGAM1179 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42309] It is yet further appreciated that a function of VGAM1179 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1179 include diagnosis, prevention and treatment of viral infection by Odontoglossum Ringspot Virus. Specific functions, and accordingly utilities, of VGAM1179 correlate with, and may be deduced from, the identity of the host target genes which VGAM1179 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42310] Nucleotide sequences of the VGAM1179 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1179 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1179 are further described hereinbelow with reference to Table 1.

[42311] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1179 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1179 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42312] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1179 gene, herein designated VGAM is inhibition of expression of VGAM1179 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1179 correlate with, and may be deduced from, the identity of the target genes which VGAM1179 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42313] ARPP-19 (Accession NM_006628) is a VGAM1179 host target gene. ARPP-19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARPP-19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-19 BINDING SITE, designated SEQ ID:13417, to the nucleotide sequence of VGAM1179 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3890.

[42314] A function of VGAM1179 is therefore inhibition of ARPP-19 (Accession NM_006628). Accordingly, utilities of VGAM1179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-19. LOC51141 (Accession XM_043953) is another VGAM1179 host target gene. LOC51141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51141 BINDING SITE, designated SEQ ID:34051, to the nucleotide sequence of VGAM1179 RNA, herein designated VGAM RNA, also designated SEQ ID:3890.

[42315] Another function of VGAM1179 is therefore inhibition of LOC51141 (Accession XM_043953). Accordingly, utilities of VGAM1179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51141. LOC91050 (Accession XM_035703) is another VGAM1179 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32332, to the nucleotide sequence of VGAM1179 RNA, herein designated VGAM RNA, also designated SEQ ID:3890.

[42316] Another function of VGAM1179 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities of VGAM1179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1180 (VGAM1180) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42317] VGAM1180 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1180 was detected is described hereinabove with reference to Figs. 1-8.

[42318] VGAM1180 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Odontoglossum*

Ringspot Virus. VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42319] VGAM1180 gene encodes a VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1180 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1180 precursor RNA is designated SEQ ID:1166, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1166 is located at position 2834 relative to the genome of Odontoglossum Ringspot Virus.

[42320] VGAM1180 precursor RNA folds onto itself, forming VGAM1180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42321] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1180 folded precursor RNA into VGAM1180 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1180 RNA is designated SEQ ID:3891, and is provided hereinbelow with reference to the sequence listing part.

[42322] VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1180 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42323] VGAM1180 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1180 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1180 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42324] The complementary binding of VGAM1180 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1180 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1180 host target RNA into VGAM1180 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42325] It is appreciated that VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1180 host target genes. The mRNA of each one of this plurality of VGAM1180 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1180 RNA, herein designated VGAM RNA, and which when bound by VGAM1180 RNA causes inhibition of translation of respective one or more VGAM1180 host target proteins.

[42326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1180 gene, herein designated VGAM GENE, on one or more VGAM1180 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42327] It is yet further appreciated that a function of VGAM1180 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of viral infection by Odontoglossum Ringspot Virus. Specific functions, and accordingly utilities, of VGAM1180 correlate with, and may be deduced from, the identity of the host target genes which VGAM1180 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42328] Nucleotide sequences of the VGAM1180 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1180 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1180 are further described hereinbelow with reference to Table 1.

[42329] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1180 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1180 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42330] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1180 gene, herein designated VGAM is inhibition of expression of VGAM1180 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1180 correlate with, and may be deduced from, the identity of the target genes which VGAM1180 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42331] ATPase, H⁺ Transporting, Lysosomal 13kDa, V1 Subunit G Isoform 2 (ATP6V1G2, Accession NM_130463) is a VGAM1180 host target gene. ATP6V1G2 BINDING SITE1 and ATP6V1G2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ATP6V1G2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ATP6V1G2 BINDING SITE1 and ATP6V1G2 BINDING SITE2, designated SEQ ID:28225 and SEQ ID:28698 respectively, to the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, also designated SEQ ID:3891.

[42332] A function of VGAM1180 is therefore inhibition of ATPase, H⁺ Transporting, Lysosomal 13kDa, V1 Subunit G Isoform 2 (ATP6V1G2, Accession NM_130463). Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1G2. Major Histocompatibility Complex, Class II, DQ Alpha 1 (HLA-DQA1, Accession XM_175260) is another VGAM1180 host target gene. HLA-DQA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLA-DQA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLA-DQA1 BINDING SITE, designated SEQ ID:46726, to the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, also designated SEQ ID:3891.

[42333] Another function of VGAM1180 is therefore inhibition of Major Histocompatibility Complex, Class II, DQ Alpha 1

(HLA-DQA1, Accession XM_175260), a gene which is alpha 1 chain of HLA-DQ1 class II molecule (Ia antigen) which binds peptides and presents them to CD4+ T lymphocytes. Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLA-DQA1. The function of HLA-DQA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132.CG018 (Accession NM_052818) is another VGAM1180 host target gene. CG018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CG018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG018 BINDING SITE, designated SEQ ID:27405, to the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, also designated SEQ ID:3891.

[42334] Another function of VGAM1180 is therefore inhibition of CG018 (Accession NM_052818). Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG018.

E2F Transcription Factor 6 (E2F6, Accession NM_001952) is another VGAM1180 host target gene. E2F6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2F6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2F6 BINDING SITE, designated SEQ ID:7676, to the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, also designated SEQ ID:3891.

[42335] Another function of VGAM1180 is therefore inhibition of E2F Transcription Factor 6 (E2F6, Accession NM_001952). Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F6. FLJ10261 (Accession NM_018043) is another VGAM1180 host target gene. FLJ10261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10261 BINDING SITE, designated SEQ ID:19789, to the nucleotide sequence of VGAM1180 RNA,

herein designated VGAM RNA, also designated SEQ ID:3891.

[42336] Another function of VGAM1180 is therefore inhibition of FLJ10261 (Accession NM_018043). Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10261. LOC92573 (Accession XM_045884) is another VGAM1180 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34600, to the nucleotide sequence of VGAM1180 RNA, herein designated VGAM RNA, also designated SEQ ID:3891.

[42337] Another function of VGAM1180 is therefore inhibition of LOC92573 (Accession XM_045884). Accordingly, utilities of VGAM1180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92573. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1181 (VGAM1181) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42338] VGAM1181 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1181 was detected is described hereinabove with reference to Figs. 1-8.

[42339] VGAM1181 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Odontoglossum Ringspot Virus. VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42340] VGAM1181 gene encodes a VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1181 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1181 precursor RNA is designated SEQ ID:1167, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1167 is located at position 4926 relative to the genome of Odontoglossum Ringspot Virus.

[42341] VGAM1181 precursor RNA folds onto itself, forming VGAM1181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42342] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1181 folded precursor RNA into VGAM1181 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1181 RNA is designated SEQ ID:3892, and is provided hereinbelow with reference to the sequence listing part.

[42343] VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1181 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1181 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42344] VGAM1181 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1181 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1181 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42345] The complementary binding of VGAM1181 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1181 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1181 host target RNA into VGAM1181 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42346] It is appreciated that VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1181 host target genes. The mRNA of each one of this plurality of VGAM1181 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1181 RNA, herein designated VGAM RNA, and which when bound by VGAM1181 RNA causes inhibition of translation of respective one or more VGAM1181 host target proteins.

[42347] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1181 gene, herein designated VGAM GENE, on one or more VGAM1181 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42348] It is yet further appreciated that a function of VGAM1181 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of viral infection by Odontoglossum Ringspot Virus. Specific functions, and accordingly utilities, of VGAM1181 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1181 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42349] Nucleotide sequences of the VGAM1181 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1181 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1181 are further described hereinbelow with reference to Table 1.

[42350] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1181 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1181 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42351] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1181 gene, herein designated VGAM is inhibition of expression of VGAM1181 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1181 correlate with, and may be deduced from, the identity of the target genes which VGAM1181

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42352] FLJ14600 (Accession NM_032810) is a VGAM1181 host target gene. FLJ14600 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14600 BINDING SITE, designated SEQ ID:26576, to the nucleotide sequence of VGAM1181 RNA, herein designated VGAM RNA, also designated SEQ ID:3892.

[42353] A function of VGAM1181 is therefore inhibition of FLJ14600 (Accession NM_032810). Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14600. KIAA0596 (Accession XM_031706) is another VGAM1181 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0596 BINDING SITE, designated SEQ ID:31465, to the nucleotide sequence of VGAM1181 RNA, herein designated VGAM RNA, also designated SEQ ID:3892.

[42354] Another function of VGAM1181 is therefore inhibition of KIAA0596 (Accession XM_031706). Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. KIAA1373 (Accession XM_048195) is another VGAM1181 host target gene. KIAA1373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1373 BINDING SITE, designated SEQ ID:35123, to the nucleotide sequence of VGAM1181 RNA, herein designated VGAM RNA, also designated SEQ ID:3892.

[42355] Another function of VGAM1181 is therefore inhibition of KIAA1373 (Accession XM_048195). Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1373. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863) is another

VGAM1181 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11288, to the nucleotide sequence of VGAM1181 RNA, herein designated VGAM RNA, also designated SEQ ID:3892.

[42356] Another function of VGAM1181 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863). Accordingly, utilities of VGAM1181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1182 (VGAM1182) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42357] VGAM1182 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1182 was detected is described hereinabove with reference to Figs. 1–8.

[42358] VGAM1182 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 4. VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42359] VGAM1182 gene encodes a VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1182 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1182 precursor RNA is designated SEQ ID:1168, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1168 is located at position 110159 relative to the genome of Human Herpesvirus 4.

[42360] VGAM1182 precursor RNA folds onto itself, forming VGAM1182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42361] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1182 folded precursor RNA into VGAM1182 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1182 RNA is designated SEQ ID:3893, and is provided hereinbelow with reference to the sequence listing part.

[42362] VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1182 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42363] VGAM1182 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1182 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1182 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[42364] The complementary binding of VGAM1182 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1182 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1182 host target RNA into VGAM1182 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42365] It is appreciated that VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1182 host target genes. The mRNA of each one of this plurality of VGAM1182 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1182 RNA, herein designated VGAM RNA, and which when bound by VGAM1182 RNA causes inhibition of translation of respective one or more VGAM1182 host target proteins.

[42366] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1182 gene, herein designated VGAM GENE, on one or more VGAM1182 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42367] It is yet further appreciated that a function of VGAM1182 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1182 correlate with, and may be deduced from, the identity of the host target genes which VGAM1182 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42368] Nucleotide sequences of the VGAM1182 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1182 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1182 are further described hereinbelow with reference to Table 1.

[42369] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1182 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1182 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42370] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1182 gene, herein designated VGAM is inhibition of expression of VGAM1182 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1182 correlate with, and may be deduced from, the identity of the target genes which VGAM1182 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42371] High Mobility Group AT-hook 2 (HMGA2, Accession NM_003483) is a VGAM1182 host target gene. HMGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGA2, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGA2 BINDING SITE, designated SEQ ID:9559, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42372] A function of VGAM1182 is therefore inhibition of High Mobility Group AT-hook 2 (HMGA2, Accession NM_003483), a gene which may affect transcription and cell differentiation; shares common DNA-binding motif with other HMG HMG I/Y family members. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGA2. The function of HMGA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552. Interferon, Gamma-inducible Protein 16 (IFI16, Accession XM_048826) is another VGAM1182 host target gene. IFI16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IFI16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of IFI16 BINDING SITE, designated SEQ ID:35281, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42373] Another function of VGAM1182 is therefore inhibition of Interferon, Gamma-inducible Protein 16 (IFI16, Accession XM_048826), a gene which could have a role in the regulation of hematopoietic differentiation and controls cellular proliferation. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IFI16. The function of IFI16 has been established by previous studies. The interferons are a family of vertebrate cytokines with pleiotropic activities including antiviral effects, the regulation of cell growth and differentiation, and modulation of immune function. Interferon-gamma (IFNG; 147570) causes an increase in the expression of major histocompatibility complex (MHC) class I and class II proteins on a variety of cells, serving to enhance antigen presentation and recognition of foreign cell surface antigens by MHC-restricted cytotoxic T lymphocytes. At least 6 interferon-gamma-inducible genes located on mouse chromosome 1 were described by Choubey et al. (1989), Kingsmore et al.

(1989), and others. In the mouse, the genes mapped to a 150-kb segment of DNA, and the serum amyloid P component gene (Sap; OMIM Ref. No. 104770) mapped within approximately 450 kb of the IFN-inducible gene cluster. The erythrocyte alpha-spectrin gene (see OMIM Ref. No. 182860) was also closely linked. Trapani et al. (1992) described a human IFN-gamma-inducible gene, IFI16, which has nucleotide sequence similarity with portions of 2 of the mouse genes. A full-length cDNA clone contained a single open reading frame of 2,187 bp which encoded a putative polypeptide of 729 amino acids. IFI16 mRNA was found to be constitutively expressed in lymphoid cells and in cell lines of both the T and B lineages. By contrast, the mRNA was not expressed in cell lines that represent early stages of myeloid development, although it was inducible in 2 of these lines with interferon-gamma. Using a panel of interspecies somatic cell hybrid cell lines, Trapani et al. (1992) localized the IFI16 gene to human 1q12-qter. DNA blotting indicated that, in contrast to the mouse, IFI16 is present as a single-copy gene in the human genome.

[42374] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [42375] Kingsmore, S. F.; Snoddy, J.; Choubey, D.; Lengyel, P.; Seldin, M. F. : Physical mapping of a family of interferon-activated genes, serum amyloid P-component, and alpha-spectrin on mouse chromosome 1. Immunogenetics 30: 169-174, 1989. ; and
- [42376] Trapani, J. A.; Browne, K. A.; Dawson, M. J.; Ramsay, R. G.; Eddy, R. L.; Shows, T. B.; White, P. C.; Dupont, B. : A novel gene constitutively expressed in human lymphoid cells is induc.
- [42377] Further studies establishing the function and utilities of IFI16 are found in John Hopkins OMIM database record ID 147586, and in cited publications numbered 3688, 420 and 11161 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499) is another VGAM1182 host target gene. NEO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEO1 BINDING SITE, designated SEQ ID:8314, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA,

also designated SEQ ID:3893.

[42378] Another function of VGAM1182 is therefore inhibition of Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499), a gene which regulates the transition of undifferentiated proliferating cells to their differentiated state. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEO1. The function of NEO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM329. TIRAP (Accession NM_052887) is another VGAM1182 host target gene. TIRAP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIRAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIRAP BINDING SITE, designated SEQ ID:27473, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42379] Another function of VGAM1182 is therefore inhibition of TIRAP (Accession NM_052887), a gene which is a adapter involved in the TLR4 signaling pathway in the innate im-

mune response. Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIRAP. The function of TIRAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM189. BTB (POZ) Domain Containing 2 (BTBD2, Accession NM_017797) is another VGAM1182 host target gene. BTBD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTBD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD2 BINDING SITE, designated SEQ ID:19438, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42380] Another function of VGAM1182 is therefore inhibition of BTB (POZ) Domain Containing 2 (BTBD2, Accession NM_017797). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD2. FGD1 Family, Member 3 (FGD3, Accession XM_053487) is another

VGAM1182 host target gene. FGD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGD3 BINDING SITE, designated SEQ ID:36092, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42381] Another function of VGAM1182 is therefore inhibition of FGD1 Family, Member 3 (FGD3, Accession XM_053487). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGD3. FLJ21791 (Accession XM_028958) is another VGAM1182 host target gene. FLJ21791 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21791, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21791 BINDING SITE, designated SEQ ID:30808, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ

ID:3893.

[42382] Another function of VGAM1182 is therefore inhibition of FLJ21791 (Accession XM_028958). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21791. GBTS1 (Accession NM_145173) is another VGAM1182 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29726, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42383] Another function of VGAM1182 is therefore inhibition of GBTS1 (Accession NM_145173). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1. KIAA1257 (Accession XM_031577) is another VGAM1182 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31428, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42384] Another function of VGAM1182 is therefore inhibition of KIAA1257 (Accession XM_031577). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. SBBI26 (Accession NM_018846) is another VGAM1182 host target gene. SBBI26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SBBI26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBBI26 BINDING SITE, designated SEQ ID:20829, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42385] Another function of VGAM1182 is therefore inhibition of SBBI26 (Accession NM_018846). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SBBI26. LOC124602 (Accession XM_058829) is another VGAM1182 host target gene. LOC124602 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124602 BINDING SITE, designated SEQ ID:36756, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42386] Another function of VGAM1182 is therefore inhibition of LOC124602 (Accession XM_058829). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124602. LOC132235 (Accession XM_072302) is another VGAM1182 host target gene. LOC132235 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC132235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132235 BINDING SITE, designated SEQ ID:37479, to

the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42387] Another function of VGAM1182 is therefore inhibition of LOC132235 (Accession XM_072302). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132235. LOC158295 (Accession XM_098915) is another VGAM1182 host target gene. LOC158295 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158295 BINDING SITE, designated SEQ ID:41936, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42388] Another function of VGAM1182 is therefore inhibition of LOC158295 (Accession XM_098915). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158295. LOC200940 (Accession XM_114324) is another VGAM1182 host target gene. LOC200940 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC200940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200940 BINDING SITE, designated SEQ ID:42874, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42389] Another function of VGAM1182 is therefore inhibition of LOC200940 (Accession XM_114324). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200940. LOC201685 (Accession XM_117325) is another VGAM1182 host target gene. LOC201685 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201685, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201685 BINDING SITE, designated SEQ ID:43383, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42390] Another function of VGAM1182 is therefore inhibition of LOC201685 (Accession XM_117325). Accordingly, utilities

of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201685. LOC203397 (Accession XM_114695) is another VGAM1182 host target gene. LOC203397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203397 BINDING SITE, designated SEQ ID:43036, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42391] Another function of VGAM1182 is therefore inhibition of LOC203397 (Accession XM_114695). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203397. LOC254413 (Accession XM_173141) is another VGAM1182 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC254413 BINDING SITE, designated SEQ ID:46397, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42392] Another function of VGAM1182 is therefore inhibition of LOC254413 (Accession XM_173141). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC57228 (Accession NM_020467) is another VGAM1182 host target gene. LOC57228 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC57228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57228 BINDING SITE, designated SEQ ID:21705, to the nucleotide sequence of VGAM1182 RNA, herein designated VGAM RNA, also designated SEQ ID:3893.

[42393] Another function of VGAM1182 is therefore inhibition of LOC57228 (Accession NM_020467). Accordingly, utilities of VGAM1182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57228. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1183 (VGAM1183) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42394] VGAM1183 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1183 was detected is described hereinabove with reference to Figs. 1–8.

[42395] VGAM1183 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cactus Virus X. VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42396] VGAM1183 gene encodes a VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1183 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1183 precursor RNA is designated SEQ ID:1169, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1169 is located at position 6096 relative to the

genome of Cactus Virus X.

[42397] VGAM1183 precursor RNA folds onto itself, forming VGAM1183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42398] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1183 folded precursor RNA into VGAM1183 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1183 RNA is designated SEQ ID:3894, and is provided hereinbelow with reference to the sequence listing part.

[42399] VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1183 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[42400] VGAM1183 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1183 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1183 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42401] The complementary binding of VGAM1183 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1183 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1183 host target RNA into VGAM1183 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42402] It is appreciated that VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1183 host target genes. The mRNA of each one of this plurality of VGAM1183 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1183 RNA, herein designated VGAM RNA, and which when bound by VGAM1183 RNA causes inhibition of translation of respective one or more VGAM1183 host target proteins.

[42403] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1183 gene, herein designated VGAM GENE, on one or more VGAM1183 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42404] It is yet further appreciated that a function of VGAM1183 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of viral infection by Cactus Virus X. Specific functions, and accordingly utilities, of VGAM1183 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1183 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42405] Nucleotide sequences of the VGAM1183 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1183 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1183 are further described hereinbelow with reference to Table 1.

[42406] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1183 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1183 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42407] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1183 gene, herein designated VGAM is inhibition of expression of VGAM1183 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1183 correlate with, and may be deduced

from, the identity of the target genes which VGAM1183 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42408] Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is a VGAM1183 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7732, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42409] A function of VGAM1183 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Phosphodiesterase 4D, CAMP-specific

(phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM_056815) is another VGAM1183 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36431, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42410] Another function of VGAM1183 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Prostaglandin-endoperoxide Synthase 2

(prostaglandin G/H synthase and cyclooxygenase) (PTGS2, Accession NM_000963) is another VGAM1183 host target gene. PTGS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS2 BINDING SITE, designated SEQ ID:6682, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42411] Another function of VGAM1183 is therefore inhibition of Prostaglandin-endoperoxide Synthase 2 (prostaglandin G/H synthase and cyclooxygenase) (PTGS2, Accession NM_000963), a gene which may have a role as a major mediator of inflammation and/or a role for prostanoid signaling in activity-dependent plasticity. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS2. The function of PTGS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM292.RAD50 Homolog (*S. cere-*

visiae) (RAD50, Accession NM_005732) is another VGAM1183 host target gene. RAD50 BINDING SITE1 and RAD50 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD50, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD50 BINDING SITE1 and RAD50 BINDING SITE2, designated SEQ ID:12292 and SEQ ID:28549 respectively, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42412] Another function of VGAM1183 is therefore inhibition of RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732), a gene which is involved in dna double-strand break repair (dsbr). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD50. The function of RAD50 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132. Serine/arginine Repetitive Matrix 1 (SRRM1, Accession NM_005839) is another VGAM1183 host target

gene. SRRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRRM1 BINDING SITE, designated SEQ ID:12448, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42413] Another function of VGAM1183 is therefore inhibition of Serine/arginine Repetitive Matrix 1 (SRRM1, Accession NM_005839). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRRM1. SUV39H2 (Accession NM_024670) is another VGAM1183 host target gene. SUV39H2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUV39H2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUV39H2 BINDING SITE, designated SEQ ID:23973, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ

ID:3894.

[42414] Another function of VGAM1183 is therefore inhibition of SUV39H2 (Accession NM_024670), a gene which is involved in gene repression and the modification of position-effect-variegation. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUV39H2. The function of SUV39H2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM424. Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788) is another VGAM1183 host target gene. UBE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4A BINDING SITE, designated SEQ ID:11194, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42415] Another function of VGAM1183 is therefore inhibition of Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A,

Accession NM_004788), a gene which binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE4A. The function of UBE4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60.FLJ25422 (Accession NM_145000) is another VGAM1183 host target gene. FLJ25422 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ25422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25422 BINDING SITE, designated SEQ ID:29603, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42416] Another function of VGAM1183 is therefore inhibition of FLJ25422 (Accession NM_145000). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ25422. KIAA1254 (Accession XM_046132) is another VGAM1183 host target gene. KIAA1254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1254 BINDING SITE, designated SEQ ID:34695, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42417] Another function of VGAM1183 is therefore inhibition of KIAA1254 (Accession XM_046132). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1254. MGC3040 (Accession XM_039805) is another VGAM1183 host target gene. MGC3040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3040 BINDING SITE, designated SEQ ID:33195, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM

RNA, also designated SEQ ID:3894.

[42418] Another function of VGAM1183 is therefore inhibition of MGC3040 (Accession XM_039805). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3040. MGC32043 (Accession NM_144582) is another VGAM1183 host target gene. MGC32043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32043 BINDING SITE, designated SEQ ID:29390, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42419] Another function of VGAM1183 is therefore inhibition of MGC32043 (Accession NM_144582). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32043. OBTP (Accession NM_017601) is another VGAM1183 host target gene. OBTP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBTP, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBTP BINDING SITE, designated SEQ ID:19076, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42420] Another function of VGAM1183 is therefore inhibition of OBTP (Accession NM_017601). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBTP. Protein Tyrosine Phosphatase Type IVA, Member 1 (PTP4A1, Accession NM_003463) is another VGAM1183 host target gene. PTP4A1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTP4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A1 BINDING SITE, designated SEQ ID:9530, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42421] Another function of VGAM1183 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 1

(PTP4A1, Accession NM_003463). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A1. RRN3 (Accession NM_018427) is another VGAM1183 host target gene. RRN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRN3 BINDING SITE, designated SEQ ID:20487, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42422] Another function of VGAM1183 is therefore inhibition of RRN3 (Accession NM_018427). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRN3. LOC150848 (Accession XM_097959) is another VGAM1183 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41256, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42423] Another function of VGAM1183 is therefore inhibition of LOC150848 (Accession XM_097959). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150848. LOC161734 (Accession XM_102109) is another VGAM1183 host target gene. LOC161734 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC161734, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161734 BINDING SITE, designated SEQ ID:42110, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42424] Another function of VGAM1183 is therefore inhibition of LOC161734 (Accession XM_102109). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161734. LOC220930 (Accession XM_167624) is an-

other VGAM1183 host target gene. LOC220930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220930 BINDING SITE, designated SEQ ID:44734, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42425] Another function of VGAM1183 is therefore inhibition of LOC220930 (Accession XM_167624). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220930. LOC221663 (Accession XM_168131) is another VGAM1183 host target gene. LOC221663 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221663 BINDING SITE, designated SEQ ID:45038, to the nucleotide sequence of VGAM1183 RNA, herein designated VGAM RNA, also designated SEQ ID:3894.

[42426] Another function of VGAM1183 is therefore inhibition of LOC221663 (Accession XM_168131). Accordingly, utilities of VGAM1183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221663. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1184 (VGAM1184) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42427] VGAM1184 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1184 was detected is described hereinabove with reference to Figs. 1–8.

[42428] VGAM1184 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cactus Virus X. VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42429] VGAM1184 gene encodes a VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1184 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1184 precursor RNA is designated SEQ ID:1170, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1170 is located at position 5274 relative to the genome of Cactus Virus X.

- [42430] VGAM1184 precursor RNA folds onto itself, forming VGAM1184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [42431] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1184 folded precursor RNA into VGAM1184 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1184 RNA is designated SEQ ID:3895, and is provided hereinbelow with reference to the sequence listing part.

[42432] VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1184 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42433] VGAM1184 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1184 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1184 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42434] The complementary binding of VGAM1184 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1184 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1184 host target RNA into VGAM1184 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42435] It is appreciated that VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1184 host target genes. The mRNA of each one of this plurality of VGAM1184 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1184 RNA, herein designated VGAM RNA, and which when bound by VGAM1184 RNA causes inhibition of translation of respective one or more VGAM1184 host target proteins.

[42436] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1184 gene, herein designated VGAM GENE, on one or more VGAM1184 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42437] It is yet further appreciated that a function of VGAM1184 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of viral infection by Cactus Virus X. Specific functions, and accordingly utilities, of VGAM1184 correlate with, and may be deduced from, the identity of the host target genes which VGAM1184 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42438] Nucleotide sequences of the VGAM1184 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1184 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1184 are further described hereinbelow with reference to Table 1.

[42439] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1184 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1184 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[42440] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1184 gene, herein designated VGAM is inhibition of expression of VGAM1184 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1184 correlate with, and may be deduced from, the identity of the target genes which VGAM1184 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42441] Fibroblast Growth Factor Receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2, Accession NM_022973) is a VGAM1184 host target gene. FGFR2 BINDING SITE1 through FGFR2 BINDING SITE11 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR2 BINDING SITE1 through FGFR2 BINDING SITE11, designated SEQ ID:23246, SEQ ID:23248, SEQ ID:23239, SEQ ID:23249, SEQ ID:23295, SEQ ID:5639, SEQ ID:23235, SEQ ID:23242, SEQ ID:23247, SEQ ID:23289

and SEQ ID:23301 respectively, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42442] A function of VGAM1184 is therefore inhibition of Fibroblast Growth Factor Receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2, Accession NM_022973). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR2. HSJ1 (Accession NM_006736) is another VGAM1184 host target gene. HSJ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSJ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSJ1 BINDING SITE, designated SEQ ID:13587, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42443] Another function of VGAM1184 is therefore inhibition of HSJ1 (Accession NM_006736). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with HSJ1. KIAA0802 (Accession XM_031357) is another VGAM1184 host target gene. KIAA0802 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0802 BINDING SITE, designated SEQ ID:31349, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42444] Another function of VGAM1184 is therefore inhibition of KIAA0802 (Accession XM_031357). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0802. I(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM_114201) is another VGAM1184 host target gene. L3MBTL2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by L3MBTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of L3MBTL2 BINDING SITE, designated SEQ

ID:42789, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42445] Another function of VGAM1184 is therefore inhibition of I(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM_114201). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L3MBTL2. LAP1B (Accession XM_035429) is another VGAM1184 host target gene. LAP1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LAP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAP1B BINDING SITE, designated SEQ ID:32261, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42446] Another function of VGAM1184 is therefore inhibition of LAP1B (Accession XM_035429). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAP1B. Serine/threonine Kinase 38 Like (STK38L, Accession

XM_044823) is another VGAM1184 host target gene.

STK38L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38L BINDING SITE, designated SEQ ID:34285, to the nucleotide sequence of VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42447] Another function of VGAM1184 is therefore inhibition of Serine/threonine Kinase 38 Like (STK38L, Accession XM_044823). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK38L. LOC149182 (Accession XM_097605) is another VGAM1184 host target gene. LOC149182 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149182 BINDING SITE, designated SEQ ID:40967, to the nucleotide sequence of

VGAM1184 RNA, herein designated VGAM RNA, also designated SEQ ID:3895.

[42448] Another function of VGAM1184 is therefore inhibition of LOC149182 (Accession XM_097605). Accordingly, utilities of VGAM1184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149182. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1185 (VGAM1185) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42449] VGAM1185 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1185 was detected is described hereinabove with reference to Figs. 1–8.

[42450] VGAM1185 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cactus Virus X.

VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42451] VGAM1185 gene encodes a VGAM1185 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1185 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1185 precursor RNA is designated SEQ ID:1171, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1171 is located at position 4689 relative to the genome of Cactus Virus X.

[42452] VGAM1185 precursor RNA folds onto itself, forming VGAM1185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42453] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1185 folded precursor RNA into VGAM1185 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1185 RNA is designated SEQ ID:3896, and is provided hereinbelow with reference to the sequence listing part.

[42454] VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1185 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42455] VGAM1185 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1185 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1185 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42456] The complementary binding of VGAM1185 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1185 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1185 host target RNA into VGAM1185 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42457] It is appreciated that VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1185 host target genes. The mRNA of each one of this plurality of VGAM1185 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1185 RNA, herein designated VGAM RNA, and which when bound by VGAM1185 RNA causes inhibition of translation of respective one or more VGAM1185 host target proteins.

[42458] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1185 gene, herein designated VGAM GENE, on one or more VGAM1185 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[42459] It is yet further appreciated that a function of VGAM1185 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of viral infection by Cactus Virus X. Specific functions, and accordingly utilities, of VGAM1185 correlate with, and may be deduced from, the identity of the host target genes which VGAM1185 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42460] Nucleotide sequences of the VGAM1185 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1185 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1185 are further described hereinbelow with reference to Table 1.

[42461] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1185 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1185 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42462] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1185 gene, herein designated VGAM is inhibition of expression of VGAM1185 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1185 correlate with, and may be deduced from, the identity of the target genes which VGAM1185 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42463] Adducin 2 (beta) (ADD2, Accession NM_017482) is a VGAM1185 host target gene. ADD2 BINDING SITE1 through ADD2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADD2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADD2 BINDING SITE1 through ADD2 BINDING SITE3, designated SEQ ID:18933, SEQ ID:18938 and SEQ ID:18946 respectively, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42464] A function of VGAM1185 is therefore inhibition of Adducin 2 (beta) (ADD2, Accession NM_017482), a gene which membrane-cytoskeleton- protein that promotes the assembly of the spectrin-actin network. Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADD2. The function of ADD2 has been established by previous studies. See alpha-adducin (ADD1; 102680). Adducin is a heterodimeric calmodulin (OMIM Ref. No. 114180)-binding protein of the cell-membrane skeleton, which is thought to play a role in assembly of the spectrin-actin lattice that underlies the plasma membrane (see OMIM Ref. No. also 182860 and 102560). Missense mutations in both the alpha- and beta-adducin genes that alter amino acids that are normally phosphorylated have been associated with the regulation of blood pressure in the Milan hypertensive strain (MHS) of rats (Bianchi et al., 1994). Muro et al. (2000) showed that in Add2 -/- mice, targeted disruption of the beta-adducin gene resulted in an 80% decrease of alpha-adducin and a 4-fold upregulation of gamma-adducin in erythrocytes. Elliptocytes, ovalocytes, and occasionally spherocytes were found in the blood smears of -/- mice. Mild hematologic findings were

thought to be related to the amount of adducin remaining in the mutant animals (presumably alpha-gamma adducin).

[42465] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42466] Bianchi, G.; Tripodi, G.; Casari, G.; Salardi, S.; Barber, B. R.; Garcia, R.; Leoni, P.; Torielli, L.; Cusi, D.; Ferrandi, M.; Pinna, L. A.; Baralle, F. E.; Ferrari, P. : Two point mutations within the adducin genes are involved in blood pressure variation. Proc. Nat. Acad. Sci. 91: 3999–4003, 1994. ; and

[42467] Muro, A. F.; Marro, M. L.; Gajovic, S.; Porro, F.; Luzzatto, L.; Baralle, F. E. : Mild spherocytic hereditary elliptocytosis and altered levels of alpha- and gamma-adducins in beta-adduc.

[42468] Further studies establishing the function and utilities of ADD2 are found in John Hopkins OMIM database record ID 102681, and in cited publications numbered 79 and 2791–488 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 7-dehydrocholesterol Reductase (DHCR7, Accession NM_001360) is another VGAM1185 host target gene.

DHCR7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DHCR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHCR7 BINDING SITE, designated SEQ ID:7040, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42469] Another function of VGAM1185 is therefore inhibition of 7-dehydrocholesterol Reductase (DHCR7, Accession NM_001360). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHCR7. Lysophospholipase I (LYPLA1, Accession NM_006330) is another VGAM1185 host target gene. LYPLA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LYPLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LYPLA1 BINDING SITE, designated SEQ ID:13028, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3896.

[42470] Another function of VGAM1185 is therefore inhibition of Lysophospholipase I (LYPLA1, Accession NM_006330). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LYPLA1. Matrix Metalloproteinase 19 (MMP19, Accession NM_002429) is another VGAM1185 host target gene. MMP19 BINDING SITE1 and MMP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE1 and MMP19 BINDING SITE2, designated SEQ ID:8268 and SEQ ID:23076 respectively, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42471] Another function of VGAM1185 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_002429). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. Phosphoribosyl Pyrophosphate Amidotransferase (PPAT, Accession

NM_002703) is another VGAM1185 host target gene.

PPAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPAT BINDING SITE, designated SEQ ID:8550, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42472] Another function of VGAM1185 is therefore inhibition of Phosphoribosyl Pyrophosphate Amidotransferase (PPAT, Accession NM_002703). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPAT. Stathmin 1/oncoprotein 18 (STMN1, Accession NM_005563) is another VGAM1185 host target gene. STMN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STMN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STMN1 BINDING SITE, designated SEQ ID:12091, to the nucleotide sequence of VGAM1185 RNA,

herein designated VGAM RNA, also designated SEQ ID:3896.

[42473] Another function of VGAM1185 is therefore inhibition of Stathmin 1/oncoprotein 18 (STMN1, Accession NM_005563), a gene which prevents assembly and promotes disassembly of microtubules. Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STMN1. The function of STMN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM281. Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476) is another VGAM1185 host target gene. BTN2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A1 BINDING SITE, designated SEQ ID:27803, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42474] Another function of VGAM1185 is therefore inhibition of

Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A1. Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943) is another VGAM1185 host target gene. CLIC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC4 BINDING SITE, designated SEQ ID:15127, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42475] Another function of VGAM1185 is therefore inhibition of Chloride Intracellular Channel 4 (CLIC4, Accession NM_013943). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC4. FLJ12875 (Accession NM_024544) is another VGAM1185 host target gene. FLJ12875 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12875, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12875 BINDING SITE, designated SEQ ID:23755, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42476] Another function of VGAM1185 is therefore inhibition of FLJ12875 (Accession NM_024544). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12875. KIAA1052 (Accession NM_014956) is another VGAM1185 host target gene. KIAA1052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1052 BINDING SITE, designated SEQ ID:17312, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42477] Another function of VGAM1185 is therefore inhibition of KIAA1052 (Accession NM_014956). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1052. Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215) is another VGAM1185 host target gene. TGOLN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TGOLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGOLN2 BINDING SITE, designated SEQ ID:32026, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42478] Another function of VGAM1185 is therefore inhibition of Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGOLN2. LOC113763 (Accession NM_138434) is another VGAM1185 host target gene. LOC113763 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC113763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC113763 BINDING SITE, designated SEQ ID:28801, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42479] Another function of VGAM1185 is therefore inhibition of LOC113763 (Accession NM_138434). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113763. LOC116113 (Accession XM_166413) is another VGAM1185 host target gene. LOC116113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116113 BINDING SITE, designated SEQ ID:44286, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42480] Another function of VGAM1185 is therefore inhibition of LOC116113 (Accession XM_166413). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116113. LOC124842 (Accession XM_064333) is an-

other VGAM1185 host target gene. LOC124842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124842 BINDING SITE, designated SEQ ID:37262, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42481] Another function of VGAM1185 is therefore inhibition of LOC124842 (Accession XM_064333). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124842. LOC149271 (Accession XM_086475) is another VGAM1185 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38679, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42482] Another function of VGAM1185 is therefore inhibition of LOC149271 (Accession XM_086475). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149271. LOC150271 (Accession XM_097859) is another VGAM1185 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41167, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42483] Another function of VGAM1185 is therefore inhibition of LOC150271 (Accession XM_097859). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC152573 (Accession XM_087488) is another VGAM1185 host target gene. LOC152573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152573, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152573 BINDING SITE, designated SEQ ID:39287, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42484] Another function of VGAM1185 is therefore inhibition of LOC152573 (Accession XM_087488). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152573. LOC158158 (Accession XM_088494) is another VGAM1185 host target gene. LOC158158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158158 BINDING SITE, designated SEQ ID:39734, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42485] Another function of VGAM1185 is therefore inhibition of LOC158158 (Accession XM_088494). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158158. LOC200860 (Accession XM_117289) is another VGAM1185 host target gene. LOC200860 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200860 BINDING SITE, designated SEQ ID:43355, to the nucleotide sequence of VGAM1185 RNA, herein designated VGAM RNA, also designated SEQ ID:3896.

[42486] Another function of VGAM1185 is therefore inhibition of LOC200860 (Accession XM_117289). Accordingly, utilities of VGAM1185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200860. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1186 (VGAM1186) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42487] VGAM1186 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1186 was detected is described hereinabove with reference to Figs. 1–8.

[42488] VGAM1186 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus C. VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42489] VGAM1186 gene encodes a VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1186 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1186 precursor RNA is designated SEQ ID:1172, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1172 is located at position 30647 relative to the genome of Human Adenovirus C.

[42490] VGAM1186 precursor RNA folds onto itself, forming VGAM1186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42491] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1186 folded precursor RNA into VGAM1186 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1186 RNA is designated SEQ ID:3897, and is provided hereinbelow with reference to the sequence listing part.

[42492] VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1186 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42493] VGAM1186 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1186 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1186 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[42494] The complementary binding of VGAM1186 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1186 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1186 host target RNA into VGAM1186 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42495] It is appreciated that VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1186 host target genes. The mRNA of each one of this plurality of VGAM1186 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1186 RNA, herein designated VGAM RNA, and which when bound by VGAM1186 RNA causes inhibition of translation of respective one or more VGAM1186 host target proteins.

[42496] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1186 gene, herein designated VGAM GENE, on one or more VGAM1186 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42497] It is yet further appreciated that a function of VGAM1186 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of viral infection by Human Adenovirus C. Specific functions, and accordingly utilities, of VGAM1186 correlate with, and may be deduced from, the identity of the host target genes which VGAM1186 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42498] Nucleotide sequences of the VGAM1186 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1186 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1186 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1186 are further described hereinbelow with reference to Table 1.

[42499] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1186 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1186 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42500] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1186 gene, herein designated VGAM is inhibition of expression of VGAM1186 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1186 correlate with, and may be deduced from, the identity of the target genes which VGAM1186 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42501] Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM_096169) is a VGAM1186 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40307, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42502] A function of VGAM1186 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM_096169), a gene which hydrolyzes Ins(1,3,4,5)P4 and PtdIns(3,4,5)P3; contains an SH2-domain. Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64. Mastermind-like 1 (Drosophila) (MAML1, Accession NM_014757) is another VGAM1186 host target gene. MAML1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of MAML1 BINDING SITE, designated SEQ ID:16500, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42503] Another function of VGAM1186 is therefore inhibition of Mastermind-like 1 (Drosophila) (MAML1, Accession NM_014757), a gene which MAML1 functions as a transcriptional coactivator for Notch signaling. Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAML1. The function of MAML1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM556. Transcription Factor Dp-1 (TFDP1, Accession NM_007111) is another VGAM1186 host target gene. TFDP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFDP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFDP1 BINDING SITE, designated SEQ ID:13978, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3897.

[42504] Another function of VGAM1186 is therefore inhibition of Transcription Factor Dp-1 (TFDP1, Accession NM_007111). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFDP1. BRAG (Accession NM_014863) is another VGAM1186 host target gene. BRAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRAG BINDING SITE, designated SEQ ID:16941, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42505] Another function of VGAM1186 is therefore inhibition of BRAG (Accession NM_014863). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRAG. KIAA0820 (Accession XM_044463) is another VGAM1186 host target gene. KIAA0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0820, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0820 BINDING SITE, designated SEQ ID:34221, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42506] Another function of VGAM1186 is therefore inhibition of KIAA0820 (Accession XM_044463). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0820. KIAA0984 (Accession XM_037557) is another VGAM1186 host target gene. KIAA0984 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0984, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0984 BINDING SITE, designated SEQ ID:32646, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42507] Another function of VGAM1186 is therefore inhibition of KIAA0984 (Accession XM_037557). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0984. KIAA1858 (Accession XM_040592) is another VGAM1186 host target gene. KIAA1858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1858 BINDING SITE, designated SEQ ID:33331, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42508] Another function of VGAM1186 is therefore inhibition of KIAA1858 (Accession XM_040592). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1858. Proteasome (prosome, macropain) Inhibitor Subunit 1 (PI31) (PSMF1, Accession NM_006814) is another VGAM1186 host target gene. PSMF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSMF1 BIND-

ING SITE, designated SEQ ID:13688, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42509] Another function of VGAM1186 is therefore inhibition of Proteasome (prosome, macropain) Inhibitor Subunit 1 (PI31) (PSMF1, Accession NM_006814). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMF1. LOC115129 (Accession XM_055292) is another VGAM1186 host target gene. LOC115129 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115129 BINDING SITE, designated SEQ ID:36256, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42510] Another function of VGAM1186 is therefore inhibition of LOC115129 (Accession XM_055292). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115129. LOC255045 (Accession XM_171243) is an-

other VGAM1186 host target gene. LOC255045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255045 BINDING SITE, designated SEQ ID:46032, to the nucleotide sequence of VGAM1186 RNA, herein designated VGAM RNA, also designated SEQ ID:3897.

[42511] Another function of VGAM1186 is therefore inhibition of LOC255045 (Accession XM_171243). Accordingly, utilities of VGAM1186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255045. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1187 (VGAM1187) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42512] VGAM1187 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1187 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[42513] VGAM1187 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus C. VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42514] VGAM1187 gene encodes a VGAM1187 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1187 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1187 precursor RNA is designated SEQ ID:1173, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1173 is located at position 26479 relative to the genome of Human Adenovirus C.

[42515] VGAM1187 precursor RNA folds onto itself, forming VGAM1187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42516] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1187 folded precursor RNA into VGAM1187 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1187 RNA is designated SEQ ID:3898, and is provided hereinbelow with reference to the sequence listing part.

[42517] VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1187 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42518] VGAM1187 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1187 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1187 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1187 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42519] The complementary binding of VGAM1187 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1187 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1187 host target RNA into VGAM1187 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42520] It is appreciated that VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1187 host target genes. The mRNA of each one of this plurality of VGAM1187 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1187 RNA, herein designated VGAM RNA, and which when bound by VGAM1187 RNA causes inhibition of translation of respective one or more VGAM1187 host target proteins.

[42521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1187 gene, herein designated VGAM GENE, on one or more VGAM1187 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42522] It is yet further appreciated that a function of VGAM1187 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of viral infection by Human Adenovirus C. Specific functions, and accordingly utilities, of VGAM1187 correlate with, and may be deduced from, the identity of the host target genes which VGAM1187 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42523] Nucleotide sequences of the VGAM1187 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1187 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1187 are further described hereinbelow with reference to Table 1.

[42524] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1187 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1187 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42525] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1187 gene, herein designated VGAM is inhibition of expression of VGAM1187 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1187 correlate with, and may be deduced from, the identity of the target genes which VGAM1187 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42526] Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719) is a VGAM1187 host target gene. CACNA1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNA1C, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA1C BINDING SITE, designated SEQ ID:6380, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42527] A function of VGAM1187 is therefore inhibition of Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719), a gene which is alpha-1 subunit of DHP-sensitive calcium channels from cardiac muscle and the brain. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA1C. The function of CACNA1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM182. Calcium Channel, Voltage-dependent, Gamma Subunit 8 (CACNG8, Accession XM_050231) is another VGAM1187 host target gene. CACNG8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CACNG8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CACNG8 BINDING SITE, designated SEQ ID:35595, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42528] Another function of VGAM1187 is therefore inhibition of Calcium Channel, Voltage-dependent, Gamma Subunit 8 (CACNG8, Accession XM_050231), a gene which may stabilize the calcium channel in an inactivated (closed) state. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNG8. The function of CACNG8 has been established by previous studies. Voltage-dependent calcium channels couple membrane depolarization in a number of cellular processes. These activities are regulated by distinct channels composed of the pore-forming alpha-1 subunit (e.g., CACNA1D; 114206) and the modulatory beta (e.g., CACNB1; 114207), alpha-2/delta (e.g., CACNA2D1; 114204), and gamma (e.g., CACNG1; 114209) subunits. By database searching and analysis of BAC clones from chromosome 19 near the PRKCG gene (OMIM Ref. No. 176980), Burgess et al. (2001) identified cDNAs encoding CACNG6 (OMIM Ref. No.

606898), CACNG7 (OMIM Ref. No. 606899), and CACNG8. The deduced 414-amino acid CACNG8 protein contains 4 transmembrane segments, a highly conserved N-glycosylation site in the first extracellular loop, and, in its C terminus, conserved phosphorylation sites and a consensus target for binding by PDZ domain proteins. Burgess et al. (2001) noted that CACNG8 may contain additional N-terminal amino acids. RT-PCR analysis of 24 adult and fetal tissues detected highest expression of CACNG8 in adult and fetal brain, followed by testis, spinal cord, and mammary.

[42529] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42530] Burgess, D. L.; Gefrides, L. A.; Foreman, P. J.; Noebels, J. L. : A cluster of three novel Ca(2+) channel gamma subunit genes on chromosome 19q13.4: evolution and expression profile of the gamma subunit gene family. *Genomics* 71: 339-350, 2001. ; and

[42531] Chu, P.-J.; Robertson, H. M.; Best, P. M. : Calcium channel gamma subunits provide insights into the evolution of this gene family. *Gene* 280: 37-48, 2001.

[42532] Further studies establishing the function and utilities of

CACNG8 are found in John Hopkins OMIM database record ID 606900, and in cited publications numbered 4526–4527 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. EGF-like-domain, Multiple 3 (EGFL3, Accession XM_031401) is another VGAM1187 host target gene. EGFL3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL3 BINDING SITE, designated SEQ ID:31374, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42533] Another function of VGAM1187 is therefore inhibition of EGF-like-domain, Multiple 3 (EGFL3, Accession XM_031401). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL3. Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM_015850) is another VGAM1187 host target gene. FGFR1 BINDING SITE1

through FGFR1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR1 BINDING SITE1 through FGFR1 BINDING SITE3, designated SEQ ID:17976, SEQ ID:23370 and SEQ ID:6205 respectively, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42534] Another function of VGAM1187 is therefore inhibition of Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM_015850). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR1. Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM_000844) is another VGAM1187 host target gene. GRM7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GRM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM7 BINDING SITE,

designated SEQ ID:6517, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42535] Another function of VGAM1187 is therefore inhibition of Glutamate Receptor, Metabotropic 7 (GRM7, Accession NM_000844), a gene which is mediated by a g-protein that inhibits adenylate cyclase activity. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM7. The function of GRM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM746. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326) is another VGAM1187 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14711, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42536] Another function of VGAM1187 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326), a gene which interact with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of MAPRE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Mannose-P-dolichol Utilization Defect 1 (MPDU1, Accession NM_004870) is another VGAM1187 host target gene. MPDU1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPDU1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPDU1 BINDING SITE, designated SEQ ID:11297, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42537] Another function of VGAM1187 is therefore inhibition of Mannose-P-dolichol Utilization Defect 1 (MPDU1, Acces-

sion NM_004870), a gene which corrects the Lec15 mutant phenotype. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPDU1. The function of MPDU1 has been established by previous studies. MPD synthase (DPM1; 603503) catalyzes the synthesis of manose-P-dolichol (MPD), an essential sugar donor for glycoconjugates and an essential substrate for synthesis of glycosylphosphatidylinositols (GPIs). The Chinese hamster ovary (CHO) Lec15 and Lec35 mutant cells are defective in synthesis and utilization, respectively, of MPD. Using an expression cloning strategy, Ware and Lehrman (1996) isolated SL15 (suppressor of Lec15), a CHO cDNA that efficiently corrected the Lec15 phenotype. The SL15 cDNA also suppressed the Lec35 mutation. Sequence analysis indicated that SL15 encodes a transmembrane protein with cytosolic C and N termini. There was no significant sequence similarity between SL15 and the *S. cerevisiae* MPD synthase, leading the authors to suggest that SL15 plays a distinct role in MPD synthesis. See also DPM2 (OMIM Ref. No. 603564). Mao et al. (1998) identified an umbilical cord blood CD34-positive cell cDNA encoding the human homolog of SL15. The predicted human pro-

tein contains 247 amino acids

[42538] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42539] Mao, M.; Fu, G.; Wu, J.-S.; Zhang, Q.-H.; Zhou, J.; Kan, L.-X.; Huang, Q.-H.; He, K.-L.; Gu, B.-W.; Han, Z.-G.; Shen, Y.; Gu, J.; Yu, Y.-P.; Xu, S.-H.; Wang, Y.-X.; Chen, S.-J.; Chen, Z. : Identification of genes expressed in human CD34+ hematopoietic stem/progenitor cells by expressed sequence tags and efficient full-length cDNA cloning. Proc. Nat. Acad. Sci. 95: 8175-8180, 1998. ; and

[42540] Ware, F. E.; Lehrman, M. A. : Expression cloning of a novel suppressor of the Lec15 and Lec35 glycosylation mutations of Chinese hamster ovary cells. J. Biol. Chem. 271: 13935-13938, 1996.

[42541] Further studies establishing the function and utilities of MPDU1 are found in John Hopkins OMIM database record ID 604041, and in cited publications numbered 8801 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neurexin 1 (NRXN1, Accession NM_138735) is another VGAM1187 host target gene. NRXN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

NRXN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN1 BINDING SITE, designated SEQ ID:28994, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42542] Another function of VGAM1187 is therefore inhibition of Neurexin 1 (NRXN1, Accession NM_138735), a gene which may be involved in cell recognition, cell adhesion, and mediate intracellular signaling. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN1. The function of NRXN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Plexin B2 (PLXNB2, Accession NM_012401) is another VGAM1187 host target gene. PLXNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLXNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

PLXNB2 BINDING SITE, designated SEQ ID:14776, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42543] Another function of VGAM1187 is therefore inhibition of Plexin B2 (PLXNB2, Accession NM_012401), a gene which is a novel member of the plexin family. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLXNB2. The function of PLXNB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87. Parathymosin (PTMS, Accession NM_002824) is another VGAM1187 host target gene. PTMS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTMS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTMS BINDING SITE, designated SEQ ID:8695, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42544] Another function of VGAM1187 is therefore inhibition of Parathymosin (PTMS, Accession NM_002824), a gene

which is involved in the regulation of cellular immunity. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTMS. The function of PTMS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.V-ski Sarcoma Viral Oncogene Homolog (avian) (SKI, Accession NM_003036) is another VGAM1187 host target gene. SKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKI BINDING SITE, designated SEQ ID:8987, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42545] Another function of VGAM1187 is therefore inhibition of V-ski Sarcoma Viral Oncogene Homolog (avian) (SKI, Accession NM_003036). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKI. Sequestosome 1 (SQSTM1, Accession NM_003900) is another VGAM1187

host target gene. SQSTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SQSTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SQSTM1 BINDING SITE, designated SEQ ID:9989, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42546] Another function of VGAM1187 is therefore inhibition of Sequestosome 1 (SQSTM1, Accession NM_003900), a gene which binds SH2 domain of p56lck and ubiquitin, and it is associated with a serine/threonine kinase activity. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SQSTM1. The function of SQSTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM824.TR2 (Accession XM_051264) is another VGAM1187 host target gene. TR2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TR2, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TR2 BINDING SITE, designated SEQ ID:35794, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42547] Another function of VGAM1187 is therefore inhibition of TR2 (Accession XM_051264), a gene which maintains high levels of reduced glutathione in the cytosol (by similarity). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TR2. The function of TR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM_012479) is another VGAM1187 host target gene. YWHAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YWHAG BINDING SITE, designated SEQ

ID:14858, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42548] Another function of VGAM1187 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM_012479), a gene which mediates mitogenic signals of PDGF in vascular smooth muscle cells. Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAG. The function of YWHAG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Cyclin E1 (CCNE1, Accession NM_001238) is another VGAM1187 host target gene. CCNE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCNE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNE1 BINDING SITE, designated SEQ ID:6906, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3898.

[42549] Another function of VGAM1187 is therefore inhibition of Cyclin E1 (CCNE1, Accession NM_001238). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNE1. CEP3 (Accession NM_006449) is another VGAM1187 host target gene. CEP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CEP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP3 BINDING SITE, designated SEQ ID:13156, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42550] Another function of VGAM1187 is therefore inhibition of CEP3 (Accession NM_006449). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP3. FLJ14525 (Accession NM_032800) is another VGAM1187 host target gene. FLJ14525 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14525, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14525 BINDING SITE, designated SEQ ID:26549, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42551] Another function of VGAM1187 is therefore inhibition of FLJ14525 (Accession NM_032800). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14525. FLJ20507 (Accession NM_017849) is another VGAM1187 host target gene. FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20507, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2, designated SEQ ID:19512 and SEQ ID:30220 respectively, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42552] Another function of VGAM1187 is therefore inhibition of

FLJ20507 (Accession NM_017849). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20507. KIAA0669 (Accession NM_014779) is another VGAM1187 host target gene. KIAA0669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0669 BINDING SITE, designated SEQ ID:16625, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42553] Another function of VGAM1187 is therefore inhibition of KIAA0669 (Accession NM_014779). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0669. KIAA0997 (Accession NM_014950) is another VGAM1187 host target gene. KIAA0997 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0997 BINDING SITE, designated SEQ ID:17279, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42554] Another function of VGAM1187 is therefore inhibition of KIAA0997 (Accession NM_014950). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0997. MACMARCKS (Accession NM_023009) is another VGAM1187 host target gene. MACMARCKS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MACMARCKS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MACMARCKS BINDING SITE, designated SEQ ID:23271, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42555] Another function of VGAM1187 is therefore inhibition of MACMARCKS (Accession NM_023009). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MACMARCKS. MGC10966 (Accession NM_031471) is

another VGAM1187 host target gene. MGC10966 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC10966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10966 BINDING SITE, designated SEQ ID:25537, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42556] Another function of VGAM1187 is therefore inhibition of MGC10966 (Accession NM_031471). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10966. Ornithine Decarboxylase Antizyme Inhibitor (OAZIN, Accession NM_015878) is another VGAM1187 host target gene. OAZIN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by OAZIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAZIN BINDING SITE, designated SEQ ID:18020, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3898.

[42557] Another function of VGAM1187 is therefore inhibition of Ornithine Decarboxylase Antizyme Inhibitor (OAZIN, Accession NM_015878). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAZIN. Polymerase (RNA) III (DNA directed) Polypeptide F, 39 KDa (POLR3F, Accession XM_009639) is another VGAM1187 host target gene. POLR3F BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by POLR3F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLR3F BINDING SITE, designated SEQ ID:30115, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42558] Another function of VGAM1187 is therefore inhibition of Polymerase (RNA) III (DNA directed) Polypeptide F, 39 KDa (POLR3F, Accession XM_009639). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLR3F. Ring Finger Protein 10 (RNF10, Accession

NM_014868) is another VGAM1187 host target gene.

RNF10 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RNF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF10 BINDING SITE, designated SEQ ID:16962, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42559] Another function of VGAM1187 is therefore inhibition of Ring Finger Protein 10 (RNF10, Accession NM_014868). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF10. Serine (or cysteine) Proteinase Inhibitor, Clade A (alpha-1 antiproteinase, antitrypsin), Member 1 (SERPINA1, Accession NM_000295) is another VGAM1187 host target gene. SERPINA1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SERPINA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SERPINA1 BINDING SITE, designated SEQ ID:5839, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42560] Another function of VGAM1187 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade A (alpha-1 antiproteinase, antitrypsin), Member 1 (SERPINA1, Accession NM_000295). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINA1. Torsin Family 2, Member A (TOR2A, Accession NM_130459) is another VGAM1187 host target gene. TOR2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOR2A BINDING SITE, designated SEQ ID:28220, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42561] Another function of VGAM1187 is therefore inhibition of Torsin Family 2, Member A (TOR2A, Accession NM_130459). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with TOR2A. LOC157226 (Accession XM_033876) is another VGAM1187 host target gene. LOC157226 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157226 BINDING SITE, designated SEQ ID:31976, to the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42562] Another function of VGAM1187 is therefore inhibition of LOC157226 (Accession XM_033876). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157226. LOC158373 (Accession XM_048539) is another VGAM1187 host target gene. LOC158373 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158373 BINDING SITE, designated SEQ ID:35190, to

the nucleotide sequence of VGAM1187 RNA, herein designated VGAM RNA, also designated SEQ ID:3898.

[42563] Another function of VGAM1187 is therefore inhibition of LOC158373 (Accession XM_048539). Accordingly, utilities of VGAM1187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158373. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1188 (VGAM1188) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42564] VGAM1188 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1188 was detected is described hereinabove with reference to Figs. 1–8.

[42565] VGAM1188 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus C. VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42566] VGAM1188 gene encodes a VGAM1188 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1188 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1188 precursor RNA is designated SEQ ID:1174, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1174 is located at position 27647 relative to the genome of Human Adenovirus C.

[42567] VGAM1188 precursor RNA folds onto itself, forming VGAM1188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42568] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1188 folded precursor RNA into VGAM1188 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1188 RNA is designated SEQ ID:3899, and is provided hereinbelow with reference to the sequence listing part.

[42569] VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1188 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42570] VGAM1188 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1188 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1188 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42571] The complementary binding of VGAM1188 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1188 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1188 host target RNA into VGAM1188 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42572] It is appreciated that VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1188 host target genes. The mRNA of each one of this plurality of VGAM1188 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1188 RNA, herein designated VGAM RNA, and which when bound by VGAM1188 RNA causes inhibition of translation of respective one or more VGAM1188 host target proteins.

[42573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1188 gene, herein designated VGAM GENE, on one or more VGAM1188 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[42574] It is yet further appreciated that a function of VGAM1188 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of viral infection by Human Adenovirus C. Specific functions, and accordingly utilities, of VGAM1188 correlate with, and may be deduced from, the identity of the host target genes which VGAM1188 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42575] Nucleotide sequences of the VGAM1188 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1188 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1188 are further described hereinbelow with reference to Table 1.

[42576] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1188 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1188 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42577] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1188 gene, herein designated VGAM is inhibition of expression of VGAM1188 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1188 correlate with, and may be deduced from, the identity of the target genes which VGAM1188 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42578] Dual Oxidase 1 (DUOX1, Accession NM_017434) is a VGAM1188 host target gene. DUOX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DUOX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUOX1 BINDING SITE, designated SEQ ID:18889, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42579] A function of VGAM1188 is therefore inhibition of Dual Oxidase 1 (DUOX1, Accession NM_017434), a gene which

is a component of the thyroid hydrogen peroxide generating system. Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUOX1. The function of DUOX1 has been established by previous studies. Using a probe for a leukocyte NADPH oxidase, De Deken et al. (2000) cloned a full-length DUOX1 cDNA from a primary human thyroid cell cDNA library. The deduced 1,551-amino acid protein has a calculated molecular mass of 177 kD. It contains several domains characteristic of flavoproteins including NADPH- and FAD-binding domains, and 4 specific histidines and a conserved arginine predicted to bind a heme prosthetic group. DUOX2 also contains 2 EF-hand motifs, 4 putative N-glycosylation sites, and 7 hydrophobic stretches. It shares 83% and 53% sequence similarity with DUOX2 and gp91-phox (OMIM Ref. No. 306400), respectively, and significant similarity to other NADPH oxidases. DUOX1 and DUOX2 share 53% and 61% sequence similarity, respectively, with a predicted protein in *C. elegans*. Northern blot analysis detected expression of a 5.7-kb DUOX1 transcript in cultured human thymocytes. Immunolocalization studies demonstrated that DUOX1 colocalizes with thyroperoxidase at the

supranuclear apical pole of all thyroid cells. De Deken et al. (2000) detected upregulated expression of DUOX1 and DUOX2 mRNA in cultured human thymocytes stimulated with cAMP agonists. In a study of thyroid carcinomas, Lacroix et al. (2001) showed that levels of DUOX1 and DUOX2 were maintained in parallel and were more frequently seen in neoplastic tissues expressing other thyroid differentiation markers.

[42580] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42581] De Deken, X.; Wang, D.; Many, M.-C.; Costagliola, S.; Libert, F.; Vassart, G.; Dumont, J. E.; Miot, F. : Cloning of two human thyroid cDNAs encoding new members of the NADPH oxidase family. J. Biol. Chem. 275: 23227-23233, 2000. ; and

[42582] Lacroix, L.; Nocera, M.; Mian, C.; Caillou, B.; Virion, A.; Dupuy, C.; Filetti, S.; Bidart, J. M.; Schlumberger, M. : Expression of nicotinamide adenine dinucleotide phosphate oxidase.

[42583] Further studies establishing the function and utilities of DUOX1 are found in John Hopkins OMIM database record ID 606758, and in cited publications numbered

5570–5571 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phospholipase C, Beta 2 (PLCB2, Accession NM_004573) is another VGAM1188 host target gene. PLCB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLCB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLCB2 BINDING SITE, designated SEQ ID:10917, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42584] Another function of VGAM1188 is therefore inhibition of Phospholipase C, Beta 2 (PLCB2, Accession NM_004573), a gene which is the beta 2 subunit of phospholipase C. Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLCB2. The function of PLCB2 has been established by previous studies. Phosphoinositide-specific phospholipase C (PLC) plays a major role in transmembrane signaling by catalyzing the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) and thereby gen-

erating the second messenger molecules inositol 1,4,5-trisphosphate (IP3) and diacylglycerol. Several distinct PLC enzymes have been identified in a variety of mammalian tissues. Park et al. (1992) isolated cDNAs encoding a previously uncharacterized PLC by screening a human cDNA library derived from the promyelocytic cell line HL-60 with a bovine PLC-beta-1 (PLCB1) cDNA. The 1,181-amino acid protein predicted from the human cDNAs shares 48% amino acid identity with rat Plcb1 and is similar in overall structure to Plcb1; thus, it was named PLC-beta-2 (PLCB2). PLCB2 and Plcb1 show the least sequence similarity in their C-terminal 450 amino acids. PLCB2 contains the X and Y regions conserved among PLCs, and 1 PEST sequence, a motif suggesting sensitivity of PLCB2 to proteases. Recombinant PLCB2 expressed in mammalian cells migrated as a 140-kD protein in SDS-polyacrylamide gels. Characterization of recombinant PLCB2 revealed that the catalytic activity of PLCB2 is dependent on calcium and that PLCB2 prefers phosphatidylinositol 4,5-bisphosphate to phosphatidylinositol as a substrate. Reconstitution experiments showed that alpha-q (OMIM Ref. No. 600998), which is the alpha subunit of the pertussis toxin-insensitive G protein, activates Plcb1

but not PLCB2, suggesting that receptor-dependent stimulation of these 2 PLCBs may require different G protein alpha subunits. By Southern blot analysis of a human/rodent somatic cell hybrid panel, Park et al. (1998) mapped the PLCB2 gene to chromosome 15. They localized the PLCB2 gene to 15q15 using FISH. Animal model experiments lend further support to the function of PLCB2. Li et al. (2000) described the phenotype of mice lacking Plcb2 and Plcb3 (OMIM Ref. No. 600230). The mice developed spontaneous multifocal skin ulcers usually starting at the age of 6 months or older. The lesions were localized mainly behind ears or on the neck, but sometimes also appeared on the face. The phenotype was similar to that of mice lacking Plcb3 alone.

[42585] It is appreciated that the abovementioned animal model for PLCB2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[42586] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42587] Park, D.; Jhon, D.-Y.; Kriz, R.; Knopf, J.; Rhee, S. G. : Cloning, sequencing, expression, and Gq-independent

activation of phospholipase C-beta-2. J. Biol. Chem. 267: 16048-16055, 1992. ; and

[42588] Li, Z.; Jiang, H.; Xie, W.; Zhang, Z.; Smrcka, A. V.; Wu, D. : Roles of PLC-beta-2 and -beta-3 and PI3K-gamma in chemoattractant-mediated signal transduction. Science 287: 1046-1049, 200.

[42589] Further studies establishing the function and utilities of PLCB2 are found in John Hopkins OMIM database record ID 604114, and in cited publications numbered 7429, 7864-7433, 283 and 7434 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DNA Cross-link Repair 1A (PSO2 homolog, S. cerevisiae) (DCLRE1A, Accession XM_044815) is another VGAM1188 host target gene. DCLRE1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCLRE1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCLRE1A BINDING SITE, designated SEQ ID:34281, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42590] Another function of VGAM1188 is therefore inhibition of

DNA Cross-link Repair 1A (PSO2 homolog, *S. cerevisiae*) (DCLRE1A, Accession XM_044815). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCLRE1A. FLJ22419 (Accession NM_024697) is another VGAM1188 host target gene. FLJ22419 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22419, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22419 BINDING SITE, designated SEQ ID:24008, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42591] Another function of VGAM1188 is therefore inhibition of FLJ22419 (Accession NM_024697). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22419. KIAA0930 (Accession XM_047214) is another VGAM1188 host target gene. KIAA0930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0930, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0930 BINDING SITE, designated SEQ ID:34915, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42592] Another function of VGAM1188 is therefore inhibition of KIAA0930 (Accession XM_047214). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0930. MGC35558 (Accession NM_145013) is another VGAM1188 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29619, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42593] Another function of VGAM1188 is therefore inhibition of MGC35558 (Accession NM_145013). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC35558. PHRET1 (Accession NM_021200) is another VGAM1188 host target gene. PHRET1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHRET1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHRET1 BINDING SITE, designated SEQ ID:22175, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42594] Another function of VGAM1188 is therefore inhibition of PHRET1 (Accession NM_021200). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHRET1. RIG-I (Accession NM_014314) is another VGAM1188 host target gene. RIG-I BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RIG-I, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIG-I BINDING SITE, designated SEQ ID:15614, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3899.

[42595] Another function of VGAM1188 is therefore inhibition of RIG-I (Accession NM_014314). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIG-I. Williams Beuren Syndrome Chromosome Region 20A (WBSCR20A, Accession NM_032158) is another VGAM1188 host target gene. WBSCR20A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WBSCR20A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR20A BINDING SITE, designated SEQ ID:25860, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42596] Another function of VGAM1188 is therefore inhibition of Williams Beuren Syndrome Chromosome Region 20A (WBSCR20A, Accession NM_032158). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR20A. LOC144600 (Accession XM_096639) is another VGAM1188 host target gene. LOC144600 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144600 BINDING SITE, designated SEQ ID:40447, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42597] Another function of VGAM1188 is therefore inhibition of LOC144600 (Accession XM_096639). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144600. LOC150622 (Accession XM_086960) is another VGAM1188 host target gene. LOC150622 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150622 BINDING SITE, designated SEQ ID:38997, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42598] Another function of VGAM1188 is therefore inhibition of

LOC150622 (Accession XM_086960). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150622. LOC204285 (Accession XM_115292) is another VGAM1188 host target gene. LOC204285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204285 BINDING SITE, designated SEQ ID:43090, to the nucleotide sequence of VGAM1188 RNA, herein designated VGAM RNA, also designated SEQ ID:3899.

[42599] Another function of VGAM1188 is therefore inhibition of LOC204285 (Accession XM_115292). Accordingly, utilities of VGAM1188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204285. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1189 (VGAM1189) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[42600] VGAM1189 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1189 was detected is described hereinabove with reference to Figs. 1–8.

[42601] VGAM1189 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Botrytis Virus F. VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42602] VGAM1189 gene encodes a VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1189 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1189 precursor RNA is designated SEQ ID:1175, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1175 is located at position 2597 relative to the genome of Botrytis Virus F.

[42603] VGAM1189 precursor RNA folds onto itself, forming VGAM1189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42604] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1189 folded precursor RNA into VGAM1189 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1189 RNA is designated SEQ ID:3900, and is provided hereinbelow with reference to the sequence listing part.

[42605] VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1189 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[42606] VGAM1189 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1189 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1189 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[42607] The complementary binding of VGAM1189 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1189 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1189 host target RNA into VGAM1189 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42608] It is appreciated that VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1189 host target genes. The mRNA of each one of this plurality of VGAM1189 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1189 RNA, herein designated VGAM RNA, and which when bound by VGAM1189 RNA causes inhibition of translation of respective one or more VGAM1189 host target proteins.

[42609] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1189 gene, herein designated VGAM GENE, on one

or more VGAM1189 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42610] It is yet further appreciated that a function of VGAM1189 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of viral infection by Botrytis Virus F. Specific functions, and accordingly utilities, of VGAM1189 correlate with, and may be deduced from, the identity of the host target genes which VGAM1189 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42611] Nucleotide sequences of the VGAM1189 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1189 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1189 are further described hereinbelow with reference to Table 1.

[42612] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1189 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1189 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42613] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1189 gene, herein designated VGAM is inhibition of expression of VGAM1189 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1189 correlate with, and may be deduced from, the identity of the target genes which VGAM1189 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42614] Acid Phosphatase 1, Soluble (ACP1, Accession

NM_004300) is a VGAM1189 host target gene. ACP1 BINDING SITE1 and ACP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP1 BINDING SITE1 and ACP1 BINDING SITE2, designated SEQ ID:10508 and SEQ ID:13958 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42615] A function of VGAM1189 is therefore inhibition of Acid Phosphatase 1, Soluble (ACP1, Accession NM_004300), a gene which as demonstrated in starch-gel electrophoresis. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP1. The function of ACP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. A Disintegrin and Metalloproteinase Domain 11 (ADAM11, Accession NM_002390) is another VGAM1189 host target gene. ADAM11 BINDING SITE1 and ADAM11 BINDING SITE2 are

HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAM11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM11 BINDING SITE1 and ADAM11 BINDING SITE2, designated SEQ ID:8207 and SEQ ID:38533 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42616] Another function of VGAM1189 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 11 (ADAM11, Accession NM_002390), a gene which Member of the ADAM family of zinc metalloproteases. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM11. The function of ADAM11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM387.B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707) is another VGAM1189 host target gene. BCL7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7B, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7B BINDING SITE, designated SEQ ID:7435, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42617] Another function of VGAM1189 is therefore inhibition of B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707), a gene which is of yet unknown function. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL7B. The function of BCL7B has been established by previous studies. Meng et al. (1998) constructed a physical map encompassing the 1.5-Mb region of chromosome 7q11.23 that is commonly deleted in Williams-Beuren syndrome (WBS; 194050). They identified 3 genes within this region, including BCL7B, which contains 6 exons. By EST database searching, screening of a liver cDNA library, and sequencing, they cloned a BCL7B cDNA encoding a deduced 202-amino acid protein that shows high homology to the BCL7A gene (OMIM Ref. No. 601406), which was cloned from a complex chromosomal translocation in Burkitt lymphoma cell lines. BCL7B is

highly conserved from *C. elegans* to human, suggesting that it has been conserved through evolution.

[42618] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42619] Jadayel, D. M.; Osborne, L. R.; Coignet, L. J. A.; Zani, V. J.; Tsui, L.-C.; Scherer, S. W.; Dyer, M. J. S. : The BCL7 gene family: deletion of BCL7B in Williams syndrome. *Gene* 224: 35–44, 1998. ; and

[42620] Meng, X.; Lu, X.; Li, Z.; Green, E. D.; Massa, H.; Trask, B. J.; Morris, C. A.; Keating, M. T. : Complete physical map of the common deletion region in Williams syndrome and identificat.

[42621] Further studies establishing the function and utilities of BCL7B are found in John Hopkins OMIM database record ID 605846, and in cited publications numbered 7187 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Bone Morpho-genetic Protein 1 (BMP1, Accession NM_006131) is another VGAM1189 host target gene. BMP1 BINDING SITE1 and BMP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BMP1, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP1 BINDING SITE1 and BMP1 BINDING SITE2, designated SEQ ID:12769 and SEQ ID:12772 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42622] Another function of VGAM1189 is therefore inhibition of Bone Morphogenetic Protein 1 (BMP1, Accession NM_006131), a gene which cleaves procollagens leading to formation of extracellular matrix. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP1. The function of BMP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Carnitine Acetyltransferase (CRAT, Accession NM_000755) is another VGAM1189 host target gene. CRAT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRAT BINDING SITE, designated SEQ ID:6406,

to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42623] Another function of VGAM1189 is therefore inhibition of Carnitine Acetyltransferase (CRAT, Accession NM_000755), a gene which catalyzes the reversible transfer of acyl groups from an acyl-CoA thioester to carnitine. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRAT. The function of CRAT has been established by previous studies. Carnitine acyltransferases are a group of enzymes that catalyze the reversible transfer of acyl groups from an acyl-CoA thioester to carnitine, thus forming the corresponding acylcarnitine. These enzymes can be distinguished according to their substrate specificity in carnitine palmitoyltransferase (see OMIM Ref. No. CPT1, 600528 and CPT2, 600650), carnitine octanoyltransferase (CROT; 606090), and carnitine acetyltransferase (EC 2.3.1.7). CRAT is a key enzyme for metabolic pathways involved with the control of the acyl-CoA/CoA ratio in mitochondria, peroxisomes, and endoplasmic reticulum Acetylcarnitine, which can be a precursor for acetylcholine synthesis catalyzed by choline acetyltransferase, is thought to

slow the rate of mental deterioration in Alzheimer patients, and Kalaria and Harik (1992) found decreased function of CRAT in the brain of Alzheimer patients

[42624] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42625] Kalaria, R. N.; Harik, S. I. : Carnitine acetyltransferase activity in the human brain and its microvessels is decreased in Alzheimer's disease. *Ann. Neurol.* 32: 583–586, 1992. ; and

[42626] van der Leij, F. R.; Huijkman, N. C. A.; Boomsma, C.; Kuipers, J. R. G.; Bartelds, B. : Genomics of the human carnitine acyltransferase genes. *Molec. Genet. Metab.* 71: 139–153, 2000.

[42627] Further studies establishing the function and utilities of CRAT are found in John Hopkins OMIM database record ID 600184, and in cited publications numbered 7744–7746 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cytoplasmic Linker 2 (CYLN2, Accession NM_003388) is another VGAM1189 host target gene. CYLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYLN2, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYLN2 BINDING SITE, designated SEQ ID:9422, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42628] Another function of VGAM1189 is therefore inhibition of Cytoplasmic Linker 2 (CYLN2, Accession NM_003388), a gene which associates with microtubules and dendritic lamellar bodies. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYLN2. The function of CYLN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM94. Dopamine Beta-hydroxylase (dopamine beta-monooxygenase) (DBH, Accession NM_000787) is another VGAM1189 host target gene. DBH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DBH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBH BINDING SITE, desig-

nated SEQ ID:6439, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42629] Another function of VGAM1189 is therefore inhibition of Dopamine Beta-hydroxylase (dopamine beta-monooxygenase) (DBH, Accession NM_000787), a gene which converts dopamine to norepinephrine . Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBH. The function of DBH has been established by previous studies. Dopamine beta-hydroxylase (DBH; EC 1.14.17.1), the enzyme that converts dopamine to norepinephrine, is present in the synaptic vesicles of postganglionic sympathetic neurons. Release of norepinephrine is accompanied by the simultaneous release of DBH. For this reason, it has been proposed that plasma DBH may serve as an index of sympathetic activity. Schanberg et al. (1974) found that subjects showed a wide range of values with a 'low' group and a 'high' group. The high group tended to show higher and less stable levels of blood pressure. In a twin study, Ross et al. (1973) found a higher concordance for level of DBH activity in monozygotic twins than in dizygotic twins. Ogiwara et al. (1975)

did not find a bimodal distribution for serum DBH in the population. However, highly significant correlations were found for the serum DBH of sib-sib pairs and mean parent-child pairs. No significant correlation was found for father-mother pairs. Weinshilboum et al. (1975) concluded that low serum dopamine beta-hydroxylase is recessive. Gershon and Goldin (1981) concluded that the family data are consistent with codominant inheritance. Possible linkage of DBH to ABO on chromosome 9 was indicated by a maximum lod score of 1.82 at 0.0 and 10% recombination fractions for males and females, respectively (Goldin et al., 1982). Elston et al. (1979) found a lod score of 2.32 at 0% recombination, giving a combined score of 2.32. Asamoah et al. (1987) studied DBH levels and polymorphic markers in 178 members of a family ascertained through 6 members who had myocardial infarction. The persons with infarction had lower levels of DBH than did others, 'but this difference was partly confounded with age differences.' Segregation analysis suggested that a codominant gene for DBH was segregating in the family. The largest lod score yielded by linkage analysis was 0.53 with ABO at 20% recombination. Adding this to the lod scores obtained by Elston et al. (1979) and

Goldin et al. (1982), they obtained combined lod scores of 2.49 and 2.50 at 0.0 and 10% recombination, respectively. Wilson et al. (1987, 1988) arrived at a lod score of 5.88 at a recombination fraction of 0.0 for the linkage of DBH and ABO. The DBH gene was not polymorphic in a black family. In studies using RFLPs of the DBH gene, Perry et al. (1991) found no recombination with argininosuccinate synthetase (OMIM Ref. No. 603470) and ABO blood group loci, with lod scores of 7.37 and 4.5, respectively, at $\theta = 0.0$. Using the full-length cDNA clone isolated by Lamouroux et al. (1987) from a human pheochromocytoma lambda library, Craig et al. (1988) showed by in situ hybridization that the DBH gene is located on 9q34. Pilz et al. (1992) used interspecies backcrosses to map the Dbh gene to mouse chromosome 2. Robertson et al. (1986) described a patient who appeared to have an isolated defect in the beta-hydroxylation of dopamine in peripheral nerves; see 146500. Man in't Veld et al. (1987) described a similar case in a 21-year-old woman with severe orthostatic hypotension. Ptosis, skeletal muscle hypotonia, and recurrent hypoglycemia had been noticed from early childhood. There was virtually complete loss of noradrenergic innervation but intact cholinergic function. Nora-

drenaline and adrenaline were not detectable in plasma, urine, and cerebrospinal fluid, but dopamine was 7- to 12-fold normal in plasma, 4-fold normal in urine, and 20-fold normal in CSF. Measurements of catecholamine metabolites showed further evidence for impairment of noradrenaline and adrenaline biosynthesis due to deficient dopamine beta-hydroxylation. Dopamine beta-hydroxylase was undetectable in plasma and CSF. Physiologic and pharmacologic stimuli of sympathetic neurotransmitter release caused increases in plasma dopamine rather than in plasma noradrenaline. The syndrome seemed to be caused by congenital dopamine beta-hydroxylase deficiency. There were no other affected individuals in the family, the parents were unrelated, and 2 sibs were in good health. As useful controls, 12 other patients with orthostatic hypotension, either idiopathic or due to other causes such as hereditary amyloidosis, primary amyloidosis, diabetic neuropathy, Shy-Drager syndrome, amyloidosis with multiple myeloma, were studied and found to have normal levels of dopamine in the plasma. Biaggioni and Robertson (1987) found remarkable improvement from administration of DL-dihydroxyphenylserine by mouth in 2 patients with life-

long orthostatic hypotension due to DBH deficiency. Both patients also had ptosis and nasal stuffiness all their lives. The agent bypasses the DBH deficiency since it is readily converted to noradrenaline by decarboxylation of the terminal carboxyl group. Mathias et al. (1990) described a brother and sister with long-standing symptoms of postural hypotension. In the male, erection was unaffected but ejaculation was prolonged or absent. Autonomic function tests confirmed sympathetic adrenergic failure with spared sympathetic cholinergic and intact parasympathetic function. There were no other neurologic abnormalities. Plasma dopamine was elevated, but noradrenaline and adrenaline were undetectable in the plasma, as was dopamine beta-hydroxylase activity. In perivascular cutaneous tissue, DBH immunoreactivity was absent. The parents were clinically and biochemically normal. Treatment with dihydroxyphenylserine reduced symptoms and signs of postural hypotension, increased plasma levels of noradrenaline, and, in the male, made ejaculation possible. Animal model experiments lend further support to the function of DBH. Thomas et al. (1995) used gene targeting to produce mice that lack *Dbh* and are therefore unable to synthesize noradrenaline or adrenaline. They found that in

heterozygous mothers, most homozygous embryos died in utero and only about 5% reached adulthood. Survival probably depended on catecholamine transfer across the placenta, because in homozygous mothers all embryos died in utero. Mortality was due to lack of noradrenaline in utero because it could be prevented by treatment with dihydroxyphenylserine (DOPS), a precursor that can be converted to noradrenaline in the absence of DBH. Mutant embryos had a histologic phenotype similar to that of embryos deficient in tyrosine hydroxylase suggesting that death might be due to cardiovascular failure, as was probably the case with TH-deficient embryos. Thomas and Palmiter (1997) found impaired maternal behavior in these mice with targeted disruption of the *Dbh* gene. Most heterozygous pups born to *Dbh*^{-/-} females died within several days of birth and were often found scattered within the bedding. Potential causes, including deficits in olfaction and lactation, were not apparent. A deficit in maternal behavior was confirmed by the lack of pup retrieval exhibited by *Dbh*^{-/-} virgin females. Restoration of norepinephrine shortly before but not after birth induced females that had previously abandoned their litters to act maternally. These results suggested to the authors that

norepinephrine is responsible for long-lasting changes that promote maternal behavior during both development and parturition in mice.

[42630] It is appreciated that the abovementioned animal model for DBH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[42631] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42632] Weinshilboum, R. M.; Schrott, H. G.; Raymond, F. A.; Weidman, W. H.; Elveback, L. R. : Inheritance of very low serum dopamine-beta-hydroxylase activity. *Am. J. Hum. Genet.* 27: 573-585, 1975. ; and

[42633] Mathias, C. J.; Bannister, R. B.; Cortelli, P.; Heslop, K.; Polak, J. M.; Raimbach, S.; Springall, D. R.; Watson, L. : Clinical, autonomic and therapeutic observations in two siblings.

[42634] Further studies establishing the function and utilities of DBH are found in John Hopkins OMIM database record ID 223360, and in cited publications numbered 9541-9555, 5226, 9556-9560, 3653, 5227, 9561-956 and 4567-1874 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Death Effector Domain Containing (DEDD, Accession NM_032998) is another VGAM1189 host target gene. DEDD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DEDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEDD BINDING SITE, designated SEQ ID:26879, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42635] Another function of VGAM1189 is therefore inhibition of Death Effector Domain Containing (DEDD, Accession NM_032998), a gene which intervenes in apoptosis. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEDD. The function of DEDD has been established by previous studies. By EST database searching with sequences of DED-containing proteins, Leo et al. (1998) and Stegh et al. (1998) independently identified and cloned the human DEDD cDNA. The DEDD cDNA encodes a deduced 318-amino acid protein with an N-terminal DED domain and a calculated molecular mass of

about 37 kD. Leo et al. (1998) and Stegh et al. (1998) also cloned the rat and mouse homologs, respectively, which share approximately 98% sequence identity with the human protein. Northern blot analysis detected ubiquitous expression of DEDD mRNA, but particularly abundant expression in testis. In human tissues, Leo et al. (1998) detected a 2.1-kb transcript, whereas Stegh et al. (1998) detected a 2.3-kb transcript in all tissues as well as a 4.2-kb transcript in some tissues. By in situ hybridization, Leo et al. (1998) found that rat DEDD mRNA was specifically expressed in male germ cells but not in Sertoli cells. An increase in DEDD mRNA was detected following induction of germ cell apoptosis using a GnRH (OMIM Ref. No. 152760) antagonist. By immunolocalization experiments, Stegh et al. (1998) found that human DEDD localized to the cytoplasm in a nonapoptotic human leukemic cell line, but translocated to the nucleus upon induction of apoptosis, where it colocalized with the nucleolar transcription factor UBTF (OMIM Ref. No. 600673). Through mutation analysis and transient transfection of human kidney cells, Stegh et al. (1998) found that the N terminus of DEDD induces apoptosis and the C terminus has antiapoptotic activity. Further, FADD (OMIM Ref. No. 602457), one of several

DED-containing proteins with which DEDD directly interacts in coimmunoprecipitation experiments, enhances DEDD-mediated apoptosis. Translocation of DEDD to the nuclear compartment requires caspase activation. Stegh et al. (1998) found that recombinant DEDD binds to both DNA and reconstituted mononucleosomes and inhibits rDNA transcription in a reconstituted in vitro system.

[42636] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42637] Leo, C. P.; Hsu, S. Y.; McGee, E. A.; Salanova, M.; Hsueh, A. J. W. : DEFT, a novel death effector domain-containing molecule predominantly expressed in testicular germ cells. *Endocrinology* 139: 4839–4848, 1998. ; and

[42638] Stegh, A. H.; Schickling, O.; Ehret, A.; Scaffidi, C.; Peterhansel, C.; Hofmann, T. G.; Grummt, I.; Krammer, P. H.; Peter, M. E. : DEDD, a novel death effector domain-containing protein.

[42639] Further studies establishing the function and utilities of DEDD are found in John Hopkins OMIM database record ID 606841, and in cited publications numbered 6142–6143 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.DNA

(cytosine-5-)-methyltransferase 3-like (DNMT3L, Accession NM_013369) is another VGAM1189 host target gene. DNMT3L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DNMT3L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3L BINDING SITE, designated SEQ ID:15018, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42640] Another function of VGAM1189 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3-like (DNMT3L, Accession NM_013369), a gene which plays a role in de novo methylation of CpG islands. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3L. The function of DNMT3L and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM447. Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is another VGAM1189 host target gene. DVL3 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10693, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42641] Another function of VGAM1189 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57.Ephrin-B1 (EFNB1, Accession NM_004429) is another VGAM1189 host target gene. EFNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of EFNB1 BINDING SITE, designated SEQ ID:10706, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42642] Another function of VGAM1189 is therefore inhibition of Ephrin-B1 (EFNB1, Accession NM_004429), a gene which is a transmembrane ligand of Eph-related receptor tyrosine kinases, has a role in cell adhesion. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB1. The function of EFNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390. Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_005231) is another VGAM1189 host target gene. EMS1 BINDING SITE1 and EMS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EMS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMS1 BINDING SITE1 and EMS1 BINDING SITE2,

designated SEQ ID:11736 and SEQ ID:28867 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42643] Another function of VGAM1189 is therefore inhibition of Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_005231), a gene which may contribute to the organization of cell structure. in transformed cells may contribute to cellular growth regulation and transformation. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMS1. The function of EMS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497. Endoglin (Osler-Rendu-Weber syndrome 1) (ENG, Accession NM_000118) is another VGAM1189 host target gene. ENG BINDING SITE1 and ENG BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ENG, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENG BINDING SITE1 and ENG BIND-

ING SITE2, designated SEQ ID:5593 and SEQ ID:21745 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42644] Another function of VGAM1189 is therefore inhibition of Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM_000118). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENG. Fatty Acid Amide Hydrolase (FAAH, Accession NM_024306) is another VGAM1189 host target gene. FAAH BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FAAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAAH BINDING SITE, designated SEQ ID:23597, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42645] Another function of VGAM1189 is therefore inhibition of Fatty Acid Amide Hydrolase (FAAH, Accession NM_024306), a gene which function as an electron carrier for several membrane bound oxygenases (by similarity).

Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAAH. The function of FAAH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM711. Formin-like (FMNL, Accession NM_005892) is another VGAM1189 host target gene. FMNL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FMNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMNL BINDING SITE, designated SEQ ID:12511, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42646] Another function of VGAM1189 is therefore inhibition of Formin-like (FMNL, Accession NM_005892), a gene which controls the reorganization of the actin cytoskeleton in association with Rac. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMNL. The function of FMNL and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM615.FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM_006732) is another VGAM1189 host target gene. FOSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOSB BINDING SITE, designated SEQ ID:13582, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42647] Another function of VGAM1189 is therefore inhibition of FBJ Murine Osteosarcoma Viral Oncogene Homolog B (FOSB, Accession NM_006732), a gene which interacts with jun proteins enhancing their dna binding activity. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOSB. The function of FOSB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM747.Guanine Nucleotide

Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM_002074) is another VGAM1189 host target gene. GNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB1 BINDING SITE, designated SEQ ID:7849, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42648] Another function of VGAM1189 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM_002074). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB1. Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843) is another VGAM1189 host target gene. GRM6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GRM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM6 BINDING SITE, des-

ignated SEQ ID:6506, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42649] Another function of VGAM1189 is therefore inhibition of Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM6. GTF2I Repeat Domain Containing 1 (GTF2IRD1, Accession NM_016328) is another VGAM1189 host target gene. GTF2IRD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GTF2IRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF2IRD1 BINDING SITE, designated SEQ ID:18451, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42650] Another function of VGAM1189 is therefore inhibition of GTF2I Repeat Domain Containing 1 (GTF2IRD1, Accession NM_016328). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF2IRD1. Hyperpolariza-

tion Activated Cyclic Nucleotide-gated Potassium Channel 2 (HCN2, Accession NM_001194) is another VGAM1189 host target gene. HCN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCN2 BINDING SITE, designated SEQ ID:6864, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42651] Another function of VGAM1189 is therefore inhibition of Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 2 (HCN2, Accession NM_001194), a gene which is hyperpolarization-activated cyclic nucleotide-gated cation channel 2 and may act as a pacemaker channel in the brain and the heart. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCN2. The function of HCN2 has been established by previous studies. Ludwig et al. (1999) observed that when expressed in HEK293 cells, HCN2 gives rise to hyperpolarization-activated cation currents with the hallmark fea-

tures of the native cation current. HCN2 has fast activation kinetics, and Ludwig et al. (1999) concluded that HCN2 may underlie the fast component of the cardiac hyperpolarization-activated cation current. By constructing truncation mutants, Wainger et al. (2001) demonstrated that the CNBD inhibits activation of the core transmembrane domain of HCN family members. Cyclic AMP binding relieves this inhibition. Differences in activation gating and extent of cAMP modulation between the HCN1 and HCN2 isoforms result largely from differences in the efficacy of CNBD inhibition.

[42652] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42653] Ludwig, A.; Zong, X.; Stieber, J.; Hullin, R.; Hofmann, F.; Biel, M. : Two pacemaker channels from human heart with profoundly different activation kinetics. EMBO J. 18: 2323–2329, 1999. ; and

[42654] Santoro, B.; Grant, S. G. N.; Bartsch, D.; Kandel, E. R. : Interactive cloning with the SH3 domain of N-src identifies a new brain specific ion channel protein, with homology to Eag and.

[42655] Further studies establishing the function and utilities of

HCN2 are found in John Hopkins OMIM database record ID 602781, and in cited publications numbered 7659–765 and 7658 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 2 Receptor, Beta (IL2RB, Accession NM_000878) is another VGAM1189 host target gene. IL2RB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL2RB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL2RB BINDING SITE, designated SEQ ID:6570, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42656] Another function of VGAM1189 is therefore inhibition of Interleukin 2 Receptor, Beta (IL2RB, Accession NM_000878), a gene which is involved in receptor mediated endocytosis and transduces the mitogenic signals of il-2. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL2RB. The function of IL2RB and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM450. Interleukin 6 Receptor (IL6R, Accession NM_000565) is another VGAM1189 host target gene. IL6R BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL6R BINDING SITE, designated SEQ ID:6172, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42657] Another function of VGAM1189 is therefore inhibition of Interleukin 6 Receptor (IL6R, Accession NM_000565), a gene which is essential to the regulation of the immune response, hematopoiesis, and acute-phase reactions. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL6R. The function of IL6R has been established by previous studies. Whereas the 0.9-kb IFN-beta-1 mRNA is transcribed from an intron-free IFNB1 gene located on 9p (OMIM Ref. No. 147640), IFN-beta-2 is the translation product of a 1.3-kb mRNA derived from an intron-containing IFNB2 gene not located on chromo-

some 9. The IFN-beta-2 mRNA does not cross-hybridize with IFN-beta-1 cDNA probes and vice-versa. Sehgal et al. (1986) mapped IFNB2 to chromosome 7 by means of a cDNA clone in blot-hybridization experiments on DNA from a panel of human-rodent somatic cell hybrids. Zilberstein et al. (1986) cloned cDNA for the 1.3-kb RNA designated IFNB2. Expression studies showed that the IFN-beta-2 secreted by DNA-transformed rodent cells is a processed 21-kD protein whose activity is cross-neutralized by antibodies to human IFN-beta-1 but not to alpha or gamma interferon. The biologic significance of IFN-beta-2 lies in the fact that it is induced under conditions in which IFN-beta-1 is not induced, as in metabolically stressed cells. Its induction by IL1 (OMIM Ref. No. 147720) and TNF (OMIM Ref. No. 191160) suggests that it may play a role as an autocrine mediator of some effects of these cytokines in inflammation and acute phase responses, as well as regulate cell proliferation. As discussed by Sehgal et al. (1987), IFNB2 is identical to B-cell differentiation factor (BSF2) and enhances proliferation in hybridoma/plasmacytoma cells. Hirano et al. (1986) reported the molecular cloning, structural analysis, and functional expression of cDNA encoding human BSF2. The

primary sequence of BSF2 deduced from the cDNA shows that it has 184 amino acids and is distinct from other interleukins. In addition to its antiviral activity, beta-2 interferon elicits acute phase response in liver cells and is identical to hepatocyte stimulatory factor. It also is identical to hybridoma growth factor. A subset of plasmacytoma (PCT), designated extramedullary PCT, is distinguished from multiple myeloma and solitary PCT of bone by its distribution among various tissue sites but not bone marrow. Extramedullary (extraosseous) PCTs are rare spontaneous neoplasms of mice but are readily induced in a susceptible strain, BALB/c, by treatment with pristane. The tumors develop in peritoneal granulomas and are characterized by Myc-activating t(12;15) chromosomal translocations and, most frequently, by secretion of IgA. To test directly the contribution of IL6 to PCT development, Kovalchuk et al. (2002) generated BALB/c mice carrying a widely expressed IL6 transgene. All mice exhibited lymphoproliferation and plasmacytosis. By 18 months of age, more than half developed readily transplantable PCTs in lymph nodes, Peyer patches, and sometimes spleen. These neoplasms also had the t(12;15) translocations, but remarkably, none expressed IgA. Approximately 30% of

the mice developed follicular and diffuse large cell B-cell lymphomas that often coexisted with PCTs. These findings provided a unique model of extramedullary PCT for studies on pathogenesis and treatment and suggested a role for IL6 in the genesis of germinal center-derived lymphomas

[42658] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42659] Hirano, T.; Yasukawa, K.; Harada, H.; Taga, T.; Watanabe, Y.; Matsuda, T.; Kashiwamura, S.; Nakajima, K.; Koyama, K.; Iwamatsu, A.; Tsunasawa, S.; Sakiyama, F.; Matsui, H.; Takahara, Y.; Taniguchi, T.; Kishimoto, T. : Complementary DNA for a novel human interleukin (BSF-2) that induces B lymphocytes to produce immunoglobulin. *Nature* 324: 73-76, 1986. ; and

[42660] Kovalchuk, A. L.; Kim, J. S.; Park, S. S.; Coleman, A. E.; Ward, J. M.; Morse, H. C, III; Kishimoto, T.; Potter, M.; Janz, S. : IL-6 transgenic mouse model for extraosseous plasmacytoma.

[42661] Further studies establishing the function and utilities of IL6R are found in John Hopkins OMIM database record ID 147880, and in cited publications numbered 397 and

3976 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) (ITGA4, Accession NM_000885) is another VGAM1189 host target gene. ITGA4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ITGA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA4 BINDING SITE, designated SEQ ID:6580, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42662] Another function of VGAM1189 is therefore inhibition of Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) (ITGA4, Accession NM_000885), a gene which recognizes one or more domains within the alternatively spliced cs-1 and cs-5 regions of fibronectin. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA4. The function of ITGA4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM1096. Integrin, Beta 4 (ITGB4, Accession NM_000213) is another VGAM1189 host target gene.

ITGB4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ITGB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB4 BINDING SITE, designated SEQ ID:5710, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42663] Another function of VGAM1189 is therefore inhibition of Integrin, Beta 4 (ITGB4, Accession NM_000213), a gene which plays a critical structural role in the hemidesmosome of epithelial cells. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB4. The function of ITGB4 has been established by previous studies. Integrins are transmembrane glycoprotein receptors that mediate cell-matrix or cell-cell adhesion, and transduced signals that regulate gene expression and cell growth (Vidal et al., 1995). These heterodimeric molecules consist of noncovalently linked alpha and beta subunits. Different combinations of alpha and beta polypeptides

form complexes that vary in their ligand-binding specificities. Both alpha and beta subunits display a cytoplasmic domain that interacts with the cytoskeleton (and possibly signaling molecules), a transmembrane region, and a large extracellular domain that interacts with the extracellular matrix. Leukocyte adhesion deficiency is due to a defect in the integrin beta-2 chain (OMIM Ref. No. 600065) and Glanzmann thrombasthenia (OMIM Ref. No. 273800) is also due to mutation in an integrin gene. In the human epidermis, basal keratinocytes express integrins alpha-2/beta-1, alpha-3/beta-1, and alpha-6/beta-4. The first 2 of these are located primarily at the lateral surface of these cells, suggesting a role in cell-cell interaction, whereas the third, alpha-6/beta-4, is restricted to the ventral surface opposed to the basal membrane zone, suggestive of its role in cell-matrix adhesion. Consistent with this possibility, alpha-6/beta-4 is found to be associated with the hemidesmosomes in stratified and transitional epithelia. Hemidesmosomes are dense cytoplasmic plaques that mediate the attachment of stratified squamous epithelium to the underlying dermis by connecting with the extracellular anchoring filaments of the basement membrane. Epidermolysis bullosa of the junctional Herlitz

type has been related to mutations in each of the 3 genes encoding laminin 5: LAMC2 (OMIM Ref. No. 150292), LAMB3 (OMIM Ref. No. 150310), and a third component. In a case of junctional epidermolysis bullosa associated with pyloric atresia (OMIM Ref. No. 226730), Vidal et al. (1995) found no mutation in any of these genes but identified a mutation in the ITGB4 gene; indeed, they found 2 mutations in the compound heterozygous patient (147557.0001 and 147557.0002). Nakano et al. (2001) identified 11 novel mutations in ITGB4 in patients with epidermolysis bullosa with congenital pyloric atresia. Four mutations predicted a premature termination codon and 7 were missense mutations. Of the 33 mutations reported to that time, those causing premature termination codons were associated with the lethal variant, whereas missense mutations were more prevalent in nonlethal forms. In general, indirect immunofluorescent studies of affected skin revealed negative staining for beta-4 integrin in lethal cases and positive, but attenuated, staining in non-lethal cases and correlated with clinical phenotype

[42664] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [42665] Vidal, F.; Aberdam, D.; Miquel, C.; Christiano, A. M.; Pulkkinen, L.; Uitto, J.; Ortonne, J.-P.; Meneguzzi, G. : Integrin beta-4 mutations associated with junctional epidermolysis bullosa with pyloric atresia. *Nature Genet.* 10: 229-234, 1995. ; and
- [42666] Nakano, A.; Pulkkinen, L.; Murrell, D.; Rico, J.; Lucky, A. W.; Garzon, M.; Stevens, C. A.; Robertson, S.; Pfendner, E.; Uitto, J. : Epidermolysis bullosa with congenital pyloric atresia.
- [42667] Further studies establishing the function and utilities of ITGB4 are found in John Hopkins OMIM database record ID 147557, and in cited publications numbered 4477, 4478-4479, 3 and 12517-12522 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ladinin 1 (LAD1, Accession NM_005558) is another VGAM1189 host target gene. LAD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAD1 BINDING SITE, designated SEQ ID:12085, to the nucleotide sequence of VGAM1189 RNA, herein

designated VGAM RNA, also designated SEQ ID:3900.

[42668] Another function of VGAM1189 is therefore inhibition of Ladinin 1 (LAD1, Accession NM_005558). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAD1. LIM Domain Kinase 1 (LIMK1, Accession NM_016735) is another VGAM1189 host target gene. LIMK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE, designated SEQ ID:18796, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42669] Another function of VGAM1189 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_016735). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Lipin 2 (LPIN2, Accession NM_014646) is another VGAM1189 host target gene. LPIN2 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by LPIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN2 BINDING SITE, designated SEQ ID:16061, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42670] Another function of VGAM1189 is therefore inhibition of Lipin 2 (LPIN2, Accession NM_014646). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPIN2. Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_015166) is another VGAM1189 host target gene. MLC1 BINDING SITE1 and MLC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MLC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLC1 BINDING SITE1 and MLC1 BINDING SITE2, designated SEQ ID:17522 and SEQ ID:29216 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42671] Another function of VGAM1189 is therefore inhibition of Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_015166). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLC1. Pleckstrin and Sec7 Domain Protein (PSD, Accession NM_002779) is another VGAM1189 host target gene. PSD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSD BINDING SITE, designated SEQ ID:8669, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42672] Another function of VGAM1189 is therefore inhibition of Pleckstrin and Sec7 Domain Protein (PSD, Accession NM_002779), a gene which promotes guanine-nucleotide exchange on arf6. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSD. The function of PSD and its association with various diseases and clinical conditions, has been established by previous studies, as

described hereinabove with reference to VGAM261.Parathymosin (PTMS, Accession NM_002824) is another VGAM1189 host target gene. PTMS BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTMS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTMS BINDING SITE, designated SEQ ID:8694, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42673] Another function of VGAM1189 is therefore inhibition of Parathymosin (PTMS, Accession NM_002824), a gene which is involved in the regulation of cellular immunity. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTMS. The function of PTMS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.Pvt1 Oncogene Homolog, MYC Activator (mouse) (PVT1, Accession XM_037656) is another VGAM1189 host target gene. PVT1 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by PVT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PVT1 BINDING SITE, designated SEQ ID:32661, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42674] Another function of VGAM1189 is therefore inhibition of Pvt1 Oncogene Homolog, MYC Activator (mouse) (PVT1, Accession XM_037656). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PVT1. PYGO2 (Accession XM_034083) is another VGAM1189 host target gene. PYGO2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PYGO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGO2 BINDING SITE, designated SEQ ID:31998, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42675] Another function of VGAM1189 is therefore inhibition of

PYGO2 (Accession XM_034083). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGO2. Scratch Homolog 1, Zinc Finger Protein (Drosophila) (SCRT1, Accession NM_031309) is another VGAM1189 host target gene. SCRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCRT1 BINDING SITE, designated SEQ ID:25345, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42676] Another function of VGAM1189 is therefore inhibition of Scratch Homolog 1, Zinc Finger Protein (Drosophila) (SCRT1, Accession NM_031309), a gene which is involved in the generation and migration of neural crest cells. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCRT1. The function of SCRT1 has been established by previous studies. Nakakura et al. (2001) isolated human SCRT from an adult brain cDNA library.

The SCRT cDNA encodes a protein of 348 amino acids. Human SCRT shares 81% and 69% identity to *Drosophila* Scrt and *Caenorhabditis elegans* neuronal antiapoptotic protein, CES-1, respectively, across the 5-zinc finger domain, and 92% overall amino acid identity with mouse Scrt. Northern blot analysis detected SCRT expression in adult brain, but not in other tissues. In situ hybridization of mouse tissues demonstrated expression of Scrt predominantly confined to the brain and spinal cord, appearing in newly differentiating, postmitotic neurons and persisting into postnatal life. Additional expression was seen in the retina and, significantly, in neuroendocrine cells of the lung. In a parallel fashion, Nakakura et al. (2001) detected SCRT expression by RT-PCR in lung cancers with neuroendocrine features, especially small cell lung cancer. SCRT shares the capacity of other Snail family members to bind to E-box enhancer motifs, which are targets of basic helix-loop-helix (bHLH) transcription factors. Nakakura et al. (2001) showed that SCRT directly antagonizes the function of heterodimers of the proneural bHLH protein achaete-scute homolog-1 (ASCL1; 100790) and E12 (see OMIM Ref. No. 147141), leading to active transcriptional repression at E-box motifs. Nakakura et al. (2001) con-

cluded that SCRT has the potential to function in newly differentiating, postmitotic neurons and in cancers with neuroendocrine features by modulating the action of bHLH transcription factors critical for neuronal differentiation.

[42677] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42678] Nakakura, E. K.; Watkins, D. N.; Schuebel, K. E.; Sriuranpong, V.; Borges, M. W.; Nelkin, B. D.; Ball, D. W. : Mammalian Scratch: a neural-specific Snail family transcriptional repressor. *Proc. Nat. Acad. Sci.* 98: 4010–4015, 2001. ; and

[42679] Scott, A. F. : Personal Communication. Baltimore, Md., 6/21/2001.

[42680] Further studies establishing the function and utilities of SCRT1 are found in John Hopkins OMIM database record ID 605858, and in cited publications numbered 6780–6781 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598) is another VGAM1189 host target gene. SLC12A7 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC12A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A7 BINDING SITE, designated SEQ ID:13373, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42681] Another function of VGAM1189 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598), a gene which is a potassium/chloride-cotransporter. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A7. The function of SLC12A7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Solute Carrier Family 6 (neurotransmitter transporter, creatine), Member 8 (SLC6A8, Accession NM_005629) is another VGAM1189 host target gene. SLC6A8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC6A8, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A8 BINDING SITE, designated SEQ ID:12146, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42682] Another function of VGAM1189 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, creatine), Member 8 (SLC6A8, Accession NM_005629). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A8. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM1189 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE, designated SEQ ID:11063, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42683] Another function of VGAM1189 is therefore inhibition of

Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Transcription Factor 1, Hepatic; LF-B1, Hepatic Nuclear Factor (HNF1), Albumin Proximal Factor (TCF1, Accession NM_000545) is another VGAM1189 host target gene. TCF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF1 BINDING SITE, designated SEQ ID:6145, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42684] Another function of VGAM1189 is therefore inhibition of Transcription Factor 1, Hepatic; LF-B1, Hepatic Nuclear Factor (HNF1), Albumin Proximal Factor (TCF1, Accession

NM_000545), a gene which is required for the expression of several liver specific genes. binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF1. The function of TCF1 has been established by previous studies. The orderly and sequential activation of genes during development is thought to be related to the selective expression of groups of regulatory proteins acting primarily at the level of transcription. Courtois et al. (1987) found a nuclear protein in hepatocytes, but not in other cell types, that binds to a sequence required for hepatocyte-specific transcription of the genes for the alpha and beta chains of fibrinogen (134820, 134830) and alpha-1-antitrypsin (OMIM Ref. No. 107400). This protein, called hepatocyte nuclear factor-1 (HNF1) by them, interacts with sequences required for optimal promoter function of the genes mentioned. The promoter or enhancer regions for several viral and cellular genes not expressed in the liver did not compete for binding to these sequences. HNF1 is predominantly expressed in liver and kidney. The restricted expression of HNF1 and its selective interaction with the control regions of several liver-

specific genes suggested to Courtois et al. (1987) that it is involved in developmentally regulated gene expression in the liver. HNF1 binds to the promoters of a variety of genes that are expressed exclusively in the liver, e.g., fibrinogen-alpha and -beta, albumin (OMIM Ref. No. 103600), alpha-fetoprotein (OMIM Ref. No. 104150), alpha-1-antitrypsin, liver-type pyruvate kinase (OMIM Ref. No. 266200), transthyretin (OMIM Ref. No. 176300), aldolase B (OMIM Ref. No. 229600), and hepatitis B virus large surface protein. The amino acid sequence of HNF1 displays distant sequence homology to the homeodomains of homeotic genes (see OMIM Ref. No. 142950). Animal model experiments lend further support to the function of TCF1. Gonzalez et al. (1990) found that newborn mice homozygous for a 1.2-cM deletion of chromosome 7 do not show the increased activity of CYP2E (OMIM Ref. No. 124040), which is regulated by the transcription factor Hnf1. They suggested that the deleted region of chromosome 7 contains a gene encoding a transacting factor that is epistatic in a regulatory cascade that includes Hnf1 gene expression.

[42685] It is appreciated that the abovementioned animal model for TCF1 is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[42686] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42687] Courtois, G.; Morgan, J. G.; Campbell, L. A.; Fourel, G.; Crabtree, G. R. : Interaction of a liver-specific nuclear factor with the fibrinogen and alpha-1-antitrypsin promoters. Science 238: 688-692, 1987. ; and

[42688] Gonzalez, F. J.; Liu, S.-Y.; Kozak, C. A.; Nebert, D. W. : Decreased Hnf-1 gene expression in mice homozygous for a 1.2-centimorgan deletion on chromosome 7. DNA Cell Biol. 9: 771-776.

[42689] Further studies establishing the function and utilities of TCF1 are found in John Hopkins OMIM database record ID 142410, and in cited publications numbered 4979, 5201-435, 12032-448, 4365-450, 11556-1155 and 12288-11564 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202) is another VGAM1189 host target gene. TCF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by TCF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF7 BINDING SITE, designated SEQ ID:9192, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42690] Another function of VGAM1189 is therefore inhibition of Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF7. Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660) is another VGAM1189 host target gene. TGFB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB1 BINDING SITE, designated SEQ ID:6319, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42691] Another function of VGAM1189 is therefore inhibition of Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB1. Tumor Necrosis Factor, Alpha-induced Protein 2 (TNFAIP2, Accession NM_006291) is another VGAM1189 host target gene. TNFAIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFAIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFAIP2 BINDING SITE, designated SEQ ID:12981, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42692] Another function of VGAM1189 is therefore inhibition of Tumor Necrosis Factor, Alpha-induced Protein 2 (TNFAIP2, Accession NM_006291). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFAIP2. Upstream Binding Transcription Factor, RNA Polymerase I (UBTF, Accession NM_014233) is another

VGAM1189 host target gene. UBTF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBTF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBTF BINDING SITE, designated SEQ ID:15496, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42693] Another function of VGAM1189 is therefore inhibition of Upstream Binding Transcription Factor, RNA Polymerase I (UBTF, Accession NM_014233), a gene which recognizes the ribosomal rna gene promoter and activates transcription. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBTF. The function of UBTF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM626. Zinc Finger Protein 42 (myeloid-specific retinoic acid- responsive) (ZNF42, Accession NM_003422) is another VGAM1189 host target gene. ZNF42 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by ZNF42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF42 BINDING SITE, designated SEQ ID:9466, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42694] Another function of VGAM1189 is therefore inhibition of Zinc Finger Protein 42 (myeloid-specific retinoic acid-responsive) (ZNF42, Accession NM_003422), a gene which may be one regulator of transcriptional events during hemopoietic development. Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF42. The function of ZNF42 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.1-acylglycerol-3-phosphate O-acyltransferase 1 (lysophosphatidic acid acyltransferase, alpha) (AGPAT1, Accession NM_006411) is another VGAM1189 host target gene. AGPAT1 BINDING SITE1 and AGPAT1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AG-

PAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGPAT1 BINDING SITE1 and AGPAT1 BINDING SITE2, designated SEQ ID:13116 and SEQ ID:26472 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42695] Another function of VGAM1189 is therefore inhibition of 1-acylglycerol-3-phosphate O-acyltransferase 1 (lysophosphatidic acid acyltransferase, alpha) (AGPAT1, Accession NM_006411). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGPAT1. Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605) is another VGAM1189 host target gene. C5orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf6 BINDING SITE, designated SEQ ID:18700, to the nucleotide sequence of VGAM1189 RNA,

herein designated VGAM RNA, also designated SEQ ID:3900.

[42696] Another function of VGAM1189 is therefore inhibition of Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf6. Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175) is another VGAM1189 host target gene. C8orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf2 BINDING SITE, designated SEQ ID:14021, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42697] Another function of VGAM1189 is therefore inhibition of Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf2. Cab45 (Accession NM_016176) is another VGAM1189 host target gene.

Cab45 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Cab45, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Cab45 BINDING SITE, designated SEQ ID:18277, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42698] Another function of VGAM1189 is therefore inhibition of Cab45 (Accession NM_016176). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Cab45. Chromobox Homolog 6 (CBX6, Accession NM_014292) is another VGAM1189 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15574, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42699] Another function of VGAM1189 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM_014292). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. Cell Division Cycle Associated 4 (CDCA4, Accession NM_017955) is another VGAM1189 host target gene. CDCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDCA4 BINDING SITE, designated SEQ ID:19661, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42700] Another function of VGAM1189 is therefore inhibition of Cell Division Cycle Associated 4 (CDCA4, Accession NM_017955). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDCA4. Complexin 1 (CPLX1, Accession NM_006651) is another VGAM1189 host target gene. CPLX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by CPLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPLX1 BINDING SITE, designated SEQ ID:13447, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42701] Another function of VGAM1189 is therefore inhibition of Complexin 1 (CPLX1, Accession NM_006651). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPLX1. Cysteine-rich with EGF-like Domains 1 (CRELD1, Accession NM_015513) is another VGAM1189 host target gene. CRELD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRELD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRELD1 BINDING SITE, designated SEQ ID:17774, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42702] Another function of VGAM1189 is therefore inhibition of

Cysteine-rich with EGF-like Domains 1 (CRELD1, Accession NM_015513). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRELD1. CXYorf1 (Accession XM_088704) is another VGAM1189 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39905, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42703] Another function of VGAM1189 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734) is another VGAM1189 host target gene. DCAMKL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DCAMKL1, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCAMKL1 BINDING SITE, designated SEQ ID:11114, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42704] Another function of VGAM1189 is therefore inhibition of Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCAMKL1. DKFZp434C0328 (Accession NM_017577) is another VGAM1189 host target gene. DKFZp434C0328 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434C0328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0328 BINDING SITE, designated SEQ ID:19010, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42705] Another function of VGAM1189 is therefore inhibition of

DKFZp434C0328 (Accession NM_017577). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0328. Ephrin-A5 (EFNA5, Accession NM_001962) is another VGAM1189 host target gene. EFNA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNA5 BINDING SITE, designated SEQ ID:7685, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42706] Another function of VGAM1189 is therefore inhibition of Ephrin-A5 (EFNA5, Accession NM_001962). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNA5. FLJ10637 (Accession XM_043919) is another VGAM1189 host target gene. FLJ10637 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10637, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10637 BINDING SITE, designated SEQ ID:34042, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42707] Another function of VGAM1189 is therefore inhibition of FLJ10637 (Accession XM_043919). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10637. FLJ10700 (Accession NM_018182) is another VGAM1189 host target gene. FLJ10700 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10700 BINDING SITE, designated SEQ ID:20019, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42708] Another function of VGAM1189 is therefore inhibition of FLJ10700 (Accession NM_018182). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10700. FLJ10743 (Accession NM_018201) is another

VGAM1189 host target gene. FLJ10743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10743 BINDING SITE, designated SEQ ID:20076, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42709] Another function of VGAM1189 is therefore inhibition of FLJ10743 (Accession NM_018201). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10743. FLJ13204 (Accession NM_024761) is another VGAM1189 host target gene. FLJ13204 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13204 BINDING SITE, designated SEQ ID:24114, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42710] Another function of VGAM1189 is therefore inhibition of FLJ13204 (Accession NM_024761). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13204. FLJ13322 (Accession NM_024722) is another VGAM1189 host target gene. FLJ13322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13322 BINDING SITE, designated SEQ ID:24058, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42711] Another function of VGAM1189 is therefore inhibition of FLJ13322 (Accession NM_024722). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13322. FLJ13881 (Accession NM_024729) is another VGAM1189 host target gene. FLJ13881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13881 BINDING SITE, designated SEQ ID:24066, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42712] Another function of VGAM1189 is therefore inhibition of FLJ13881 (Accession NM_024729). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13881. FLJ14100 (Accession NM_025025) is another VGAM1189 host target gene. FLJ14100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14100 BINDING SITE, designated SEQ ID:24614, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42713] Another function of VGAM1189 is therefore inhibition of FLJ14100 (Accession NM_025025). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ14100. FLJ14327 (Accession NM_024912) is another VGAM1189 host target gene. FLJ14327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14327 BINDING SITE, designated SEQ ID:24424, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42714] Another function of VGAM1189 is therefore inhibition of FLJ14327 (Accession NM_024912). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14327. FLJ20257 (Accession NM_019606) is another VGAM1189 host target gene. FLJ20257 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20257 BINDING SITE, designated SEQ ID:21222, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM

RNA, also designated SEQ ID:3900.

[42715] Another function of VGAM1189 is therefore inhibition of FLJ20257 (Accession NM_019606). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20257. FLJ22301 (Accession NM_024836) is another VGAM1189 host target gene. FLJ22301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22301 BINDING SITE, designated SEQ ID:24240, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42716] Another function of VGAM1189 is therefore inhibition of FLJ22301 (Accession NM_024836). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22301. FLJ31300 (Accession NM_144639) is another VGAM1189 host target gene. FLJ31300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31300, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31300 BINDING SITE, designated SEQ ID:29462, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42717] Another function of VGAM1189 is therefore inhibition of FLJ31300 (Accession NM_144639). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31300. GABA(A) Receptor-associated Protein Like 1 (GABARAPL1, Accession NM_031412) is another VGAM1189 host target gene. GABARAPL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GABARAPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABARAPL1 BINDING SITE, designated SEQ ID:25390, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42718] Another function of VGAM1189 is therefore inhibition of GABA(A) Receptor-associated Protein Like 1 (GABARAPL1,

Accession NM_031412). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABARAPL1. GBTS1 (Accession NM_145173) is another VGAM1189 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29727, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42719] Another function of VGAM1189 is therefore inhibition of GBTS1 (Accession NM_145173). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1. HS6ST (Accession XM_030529) is another VGAM1189 host target gene. HS6ST BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS6ST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of HS6ST BINDING SITE, designated SEQ ID:31071, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42720] Another function of VGAM1189 is therefore inhibition of HS6ST (Accession XM_030529). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS6ST. Heparan Sulfate 6-O-sulfotransferase 1 (HS6ST1, Accession NM_004807) is another VGAM1189 host target gene. HS6ST1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS6ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS6ST1 BINDING SITE, designated SEQ ID:11229, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42721] Another function of VGAM1189 is therefore inhibition of Heparan Sulfate 6-O-sulfotransferase 1 (HS6ST1, Accession NM_004807). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with HS6ST1. HSPC195 (Accession XM_087785) is another VGAM1189 host target gene. HSPC195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC195 BINDING SITE, designated SEQ ID:39421, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42722] Another function of VGAM1189 is therefore inhibition of HSPC195 (Accession XM_087785). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC195. HYPC (Accession XM_035487) is another VGAM1189 host target gene. HYPC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HYPC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYPC BINDING SITE, designated SEQ ID:32272, to the nucleotide sequence of

VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42723] Another function of VGAM1189 is therefore inhibition of HYPC (Accession XM_035487). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYPC. ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM_047951) is another VGAM1189 host target gene. ISL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ISL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ISL2 BINDING SITE, designated SEQ ID:35080, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42724] Another function of VGAM1189 is therefore inhibition of ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM_047951). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ISL2. KIAA0140 (Accession NM_014661) is another VGAM1189

host target gene. KIAA0140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0140 BINDING SITE, designated SEQ ID:16107, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42725] Another function of VGAM1189 is therefore inhibition of KIAA0140 (Accession NM_014661). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0140. KIAA0227 (Accession XM_027236) is another VGAM1189 host target gene. KIAA0227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0227 BINDING SITE, designated SEQ ID:30451, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42726] Another function of VGAM1189 is therefore inhibition of KIAA0227 (Accession XM_027236). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0227. KIAA0415 (Accession XM_166527) is another VGAM1189 host target gene. KIAA0415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0415 BINDING SITE, designated SEQ ID:44474, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42727] Another function of VGAM1189 is therefore inhibition of KIAA0415 (Accession XM_166527). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0415. KIAA0446 (Accession XM_044155) is another VGAM1189 host target gene. KIAA0446 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34148, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42728] Another function of VGAM1189 is therefore inhibition of KIAA0446 (Accession XM_044155). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0446. KIAA0481 (Accession XM_050144) is another VGAM1189 host target gene. KIAA0481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0481 BINDING SITE, designated SEQ ID:35569, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42729] Another function of VGAM1189 is therefore inhibition of KIAA0481 (Accession XM_050144). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0481. KIAA0841 (Accession XM_049237) is another VGAM1189 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35360, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42730] Another function of VGAM1189 is therefore inhibition of KIAA0841 (Accession XM_049237). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0841. KIAA0939 (Accession XM_030524) is another VGAM1189 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31060, to the nucleotide sequence of VGAM1189 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3900.

[42731] Another function of VGAM1189 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA0963 (Accession NM_014963) is another VGAM1189 host target gene. KIAA0963 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0963 BINDING SITE, designated SEQ ID:17342, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42732] Another function of VGAM1189 is therefore inhibition of KIAA0963 (Accession NM_014963). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0963. KIAA1138 (Accession XM_030721) is another VGAM1189 host target gene. KIAA1138 BINDING SITE1 and KIAA1138 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

KIAA1138, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1138 BINDING SITE1 and KIAA1138 BINDING SITE2, designated SEQ ID:31125 and SEQ ID:31126 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42733] Another function of VGAM1189 is therefore inhibition of KIAA1138 (Accession XM_030721). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1138. KIAA1441 (Accession XM_114036) is another VGAM1189 host target gene. KIAA1441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1441 BINDING SITE, designated SEQ ID:42627, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42734] Another function of VGAM1189 is therefore inhibition of

KIAA1441 (Accession XM_114036). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1441. KIAA1453 (Accession NM_025090) is another VGAM1189 host target gene. KIAA1453 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1453 BINDING SITE, designated SEQ ID:24713, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42735] Another function of VGAM1189 is therefore inhibition of KIAA1453 (Accession NM_025090). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1453. KIAA1553 (Accession XM_166320) is another VGAM1189 host target gene. KIAA1553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1553 BINDING SITE, designated SEQ ID:44142, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42736] Another function of VGAM1189 is therefore inhibition of KIAA1553 (Accession XM_166320). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1553. KIAA1580 (Accession XM_045271) is another VGAM1189 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34411, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42737] Another function of VGAM1189 is therefore inhibition of KIAA1580 (Accession XM_045271). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1813 (Accession XM_046743) is another

VGAM1189 host target gene. KIAA1813 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1813 BINDING SITE, designated SEQ ID:34808, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42738] Another function of VGAM1189 is therefore inhibition of KIAA1813 (Accession XM_046743). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1813. KIAA1893 (Accession XM_055226) is another VGAM1189 host target gene. KIAA1893 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1893 BINDING SITE, designated SEQ ID:36245, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42739] Another function of VGAM1189 is therefore inhibition of KIAA1893 (Accession XM_055226). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1893. KIAA1904 (Accession XM_056282) is another VGAM1189 host target gene. KIAA1904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE, designated SEQ ID:36373, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42740] Another function of VGAM1189 is therefore inhibition of KIAA1904 (Accession XM_056282). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. KIAA1924 (Accession XM_057091) is another VGAM1189 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36473, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42741] Another function of VGAM1189 is therefore inhibition of KIAA1924 (Accession XM_057091). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. Lectin, Galactoside-binding, Soluble, 12 (galectin 12) (LGALS12, Accession NM_033101) is another VGAM1189 host target gene. LGALS12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LGALS12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGALS12 BINDING SITE, designated SEQ ID:26947, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42742] Another function of VGAM1189 is therefore inhibition of Lectin, Galactoside-binding, Soluble, 12 (galectin 12) (LGALS12, Accession NM_033101). Accordingly, utilities of

VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGALS12. MGC10966 (Accession NM_031471) is another VGAM1189 host target gene. MGC10966 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC10966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10966 BINDING SITE, designated SEQ ID:25536, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42743] Another function of VGAM1189 is therefore inhibition of MGC10966 (Accession NM_031471). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10966. MGC2705 (Accession NM_032701) is another VGAM1189 host target gene. MGC2705 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC2705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2705

BINDING SITE, designated SEQ ID:26415, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42744] Another function of VGAM1189 is therefore inhibition of MGC2705 (Accession NM_032701). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2705. MGC2827 (Accession NM_023940) is another VGAM1189 host target gene. MGC2827 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2827 BINDING SITE, designated SEQ ID:23425, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42745] Another function of VGAM1189 is therefore inhibition of MGC2827 (Accession NM_023940). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2827. Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM_005930) is another

VGAM1189 host target gene. MGEA6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGEA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA6 BINDING SITE, designated SEQ ID:12559, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42746] Another function of VGAM1189 is therefore inhibition of Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM_005930). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGEA6. N4BP3 (Accession XM_038920) is another VGAM1189 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32932, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3900.

[42747] Another function of VGAM1189 is therefore inhibition of N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. NFASC (Accession XM_046808) is another VGAM1189 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34828, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42748] Another function of VGAM1189 is therefore inhibition of NFASC (Accession XM_046808). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. NOPAR (Accession NM_053002) is another VGAM1189 host target gene. NOPAR BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NOPAR, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOPAR BINDING SITE, designated SEQ ID:27570, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42749] Another function of VGAM1189 is therefore inhibition of NOPAR (Accession NM_053002). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOPAR. OS4 (Accession NM_005730) is another VGAM1189 host target gene. OS4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OS4 BINDING SITE, designated SEQ ID:12287, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42750] Another function of VGAM1189 is therefore inhibition of OS4 (Accession NM_005730). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with OS4.

P17.3 (Accession NM_019056) is another VGAM1189 host target gene. P17.3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by P17.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P17.3 BINDING SITE, designated SEQ ID:21138, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42751] Another function of VGAM1189 is therefore inhibition of P17.3 (Accession NM_019056). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P17.3. p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168) is another VGAM1189 host target gene. PAK6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PAK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK6 BINDING SITE, designated SEQ ID:21389,

to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42752] Another function of VGAM1189 is therefore inhibition of p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK6. Phospholipase A2, Group VI (cytosolic, calcium-independent) (PLA2G6, Accession XM_039248) is another VGAM1189 host target gene. PLA2G6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G6 BINDING SITE, designated SEQ ID:33030, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42753] Another function of VGAM1189 is therefore inhibition of Phospholipase A2, Group VI (cytosolic, calcium-independent) (PLA2G6, Accession XM_039248). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with PLA2G6. Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531) is another VGAM1189 host target gene. PRKWNK2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRKWNK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKWNK2 BINDING SITE, designated SEQ ID:43519, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42754] Another function of VGAM1189 is therefore inhibition of Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKWNK2. Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM_133177) is another VGAM1189 host target gene. PTPRU BINDING SITE1 through PTPRU BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRU, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementar-

ity of the nucleotide sequences of PTPRU BINDING SITE1 through PTPRU BINDING SITE3, designated SEQ ID:28399, SEQ ID:28404 and SEQ ID:12254 respectively, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42755] Another function of VGAM1189 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, U (PTPRU, Accession NM_133177). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRU. SEC61A1 (Accession NM_013336) is another VGAM1189 host target gene. SEC61A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC61A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC61A1 BINDING SITE, designated SEQ ID:14983, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42756] Another function of VGAM1189 is therefore inhibition of SEC61A1 (Accession NM_013336). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SEC61A1. Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379) is another VGAM1189 host target gene. SEMA3C BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SEMA3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA3C BINDING SITE, designated SEQ ID:13072, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42757] Another function of VGAM1189 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Short Basic Domain, Secreted, (semaphorin) 3C (SEMA3C, Accession NM_006379). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA3C. Stathmin-like 3 (STMN3, Accession NM_015894) is another VGAM1189 host target gene. STMN3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STMN3, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STMN3 BINDING SITE, designated SEQ ID:18037, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42758] Another function of VGAM1189 is therefore inhibition of Stathmin-like 3 (STMN3, Accession NM_015894). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STMN3. LOC115051 (Accession XM_010647) is another VGAM1189 host target gene. LOC115051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115051 BINDING SITE, designated SEQ ID:30158, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42759] Another function of VGAM1189 is therefore inhibition of LOC115051 (Accession XM_010647). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC115051. LOC144114 (Accession XM_090198) is another VGAM1189 host target gene. LOC144114 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144114 BINDING SITE, designated SEQ ID:39994, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42760] Another function of VGAM1189 is therefore inhibition of LOC144114 (Accession XM_090198). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144114. LOC146268 (Accession XM_085397) is another VGAM1189 host target gene. LOC146268 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146268 BINDING SITE, designated SEQ ID:38120, to

the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42761] Another function of VGAM1189 is therefore inhibition of LOC146268 (Accession XM_085397). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146268. LOC146488 (Accession XM_047748) is another VGAM1189 host target gene. LOC146488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE, designated SEQ ID:35042, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42762] Another function of VGAM1189 is therefore inhibition of LOC146488 (Accession XM_047748). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC146895 (Accession XM_097120) is another VGAM1189 host target gene. LOC146895 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC146895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146895 BINDING SITE, designated SEQ ID:40759, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42763] Another function of VGAM1189 is therefore inhibition of LOC146895 (Accession XM_097120). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146895. LOC157349 (Accession XM_088298) is another VGAM1189 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39589, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42764] Another function of VGAM1189 is therefore inhibition of LOC157349 (Accession XM_088298). Accordingly, utilities

of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. LOC159090 (Accession XM_088749) is another VGAM1189 host target gene. LOC159090 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC159090, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159090 BINDING SITE, designated SEQ ID:39939, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42765] Another function of VGAM1189 is therefore inhibition of LOC159090 (Accession XM_088749). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159090. LOC196500 (Accession XM_113734) is another VGAM1189 host target gene. LOC196500 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC196500 BINDING SITE, designated SEQ ID:42388, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42766] Another function of VGAM1189 is therefore inhibition of LOC196500 (Accession XM_113734). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196500. LOC199786 (Accession XM_114021) is another VGAM1189 host target gene. LOC199786 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199786 BINDING SITE, designated SEQ ID:42617, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42767] Another function of VGAM1189 is therefore inhibition of LOC199786 (Accession XM_114021). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199786. LOC199800 (Accession XM_117134) is another VGAM1189 host target gene. LOC199800 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199800 BINDING SITE, designated SEQ ID:43249, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42768] Another function of VGAM1189 is therefore inhibition of LOC199800 (Accession XM_117134). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199800. LOC200093 (Accession XM_032184) is another VGAM1189 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31597, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42769] Another function of VGAM1189 is therefore inhibition of

LOC200093 (Accession XM_032184). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC201245 (Accession XM_113326) is another VGAM1189 host target gene. LOC201245 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201245 BINDING SITE, designated SEQ ID:42229, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42770] Another function of VGAM1189 is therefore inhibition of LOC201245 (Accession XM_113326). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201245. LOC205095 (Accession XM_119820) is another VGAM1189 host target gene. LOC205095 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC205095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC205095 BINDING SITE, designated SEQ ID:43603, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42771] Another function of VGAM1189 is therefore inhibition of LOC205095 (Accession XM_119820). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205095. LOC219513 (Accession XM_169166) is another VGAM1189 host target gene. LOC219513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219513 BINDING SITE, designated SEQ ID:45291, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42772] Another function of VGAM1189 is therefore inhibition of LOC219513 (Accession XM_169166). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219513. LOC221424 (Accession XM_168060) is an-

other VGAM1189 host target gene. LOC221424 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221424, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221424 BINDING SITE, designated SEQ ID:44977, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42773] Another function of VGAM1189 is therefore inhibition of LOC221424 (Accession XM_168060). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221424. LOC222183 (Accession XM_168436) is another VGAM1189 host target gene. LOC222183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222183 BINDING SITE, designated SEQ ID:45183, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42774] Another function of VGAM1189 is therefore inhibition of LOC222183 (Accession XM_168436). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222183. LOC256867 (Accession XM_170694) is another VGAM1189 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45471, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42775] Another function of VGAM1189 is therefore inhibition of LOC256867 (Accession XM_170694). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. LOC257451 (Accession XM_170960) is another VGAM1189 host target gene. LOC257451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257451, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257451 BINDING SITE, designated SEQ ID:45741, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42776] Another function of VGAM1189 is therefore inhibition of LOC257451 (Accession XM_170960). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257451. LOC90768 (Accession XM_033986) is another VGAM1189 host target gene. LOC90768 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90768 BINDING SITE, designated SEQ ID:31986, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42777] Another function of VGAM1189 is therefore inhibition of LOC90768 (Accession XM_033986). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90768. LOC91040 (Accession XM_035641) is another VGAM1189 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32315, to the nucleotide sequence of VGAM1189 RNA, herein designated VGAM RNA, also designated SEQ ID:3900.

[42778] Another function of VGAM1189 is therefore inhibition of LOC91040 (Accession XM_035641). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. LOC91149 (Accession XM_036480) is another VGAM1189 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32455, to the nucleotide sequence of VGAM1189 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3900.

[42779] Another function of VGAM1189 is therefore inhibition of LOC91149 (Accession XM_036480). Accordingly, utilities of VGAM1189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91149. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1190 (VGAM1190) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42780] VGAM1190 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1190 was detected is described hereinabove with reference to Figs. 1–8.

[42781] VGAM1190 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Botrytis Virus F. VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42782] VGAM1190 gene encodes a VGAM1190 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1190 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1190 precursor RNA is designated SEQ ID:1176, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1176 is located at position 2147 relative to the genome of Botrytis Virus F.

[42783] VGAM1190 precursor RNA folds onto itself, forming VGAM1190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42784] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1190 folded precursor RNA into VGAM1190 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM1190 RNA is designated SEQ ID:3901, and is provided hereinbelow with reference to the sequence listing part.

[42785] VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1190 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42786] VGAM1190 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1190 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1190 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[42787] The complementary binding of VGAM1190 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1190 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1190 host target RNA into VGAM1190 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42788] It is appreciated that VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1190 host target genes. The mRNA of

each one of this plurality of VGAM1190 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1190 RNA, herein designated VGAM RNA, and which when bound by VGAM1190 RNA causes inhibition of translation of respective one or more VGAM1190 host target proteins.

[42789] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1190 gene, herein designated VGAM GENE, on one or more VGAM1190 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[42790] It is yet further appreciated that a function of VGAM1190 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of viral infection by Botrytis Virus F. Specific functions, and accordingly utilities, of VGAM1190 correlate with, and may be deduced from, the identity of the host target genes which VGAM1190 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42791] Nucleotide sequences of the VGAM1190 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1190 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1190 are further described hereinbelow with reference to Table 1.

[42792] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1190 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1190 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42793] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1190 gene, herein designated VGAM is inhibition of expression of VGAM1190 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1190 correlate with, and may be deduced from, the identity of the target genes which VGAM1190 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42794] BIG1 (Accession NM_006421) is a VGAM1190 host target gene. BIG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BIG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIG1 BINDING SITE, designated SEQ ID:13136, to the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42795] A function of VGAM1190 is therefore inhibition of BIG1 (Accession NM_006421), a gene which is a guanine nucleotide-exchange protein, has a role in vesicular transport. Accordingly, utilities of VGAM1190 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with BIG1. The function of BIG1 has been established by previous studies. After peptide sequencing of purified bovine p200, Togawa et al. (1999) used PCR generated probes to screen a human frontal cortex cDNA library and isolated BIG1 and BIG2 (OMIM Ref. No. 605371) cDNAs. The assembled full-length BIG1 cDNA encodes a protein of 1,849 amino acids containing a Sec7 domain characteristic of ARF guanine nucleotide-exchange proteins. BIG1 shares 74% overall amino acid identity with BIG2 and 90% identity in the Sec7 domain. Using Northern blot analysis, Togawa et al. (1999) detected a 7.5-kb BIG1 transcript in placenta and lung. Weaker expression was detected in heart, brain, kidney, and pancreas. Mansour et al. (1999) studied the ubiquitously expressed ARFGEP1 protein and proposed that accumulation of an abortive p200-ARF complex in the presence of BFA likely leads to disruption of Golgi morphology. Database searches revealed the presence of putative isoforms whose inhibition may account for the effects of BFA on various organelles.

[42796] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [42797] Togawa, A.; Morinaga, N.; Ogasawara, M.; Moss, J.; Vaughan, M. : Purification and cloning of a brefeldin A-inhibited guanine nucleotide-exchange protein for ADP-ribosylation factors. J. Biol. Chem. 274: 12308-12315, 1999. ; and
- [42798] Mansour, S. J.; Skaug, J.; Zhao, X.-H.; Giordano, J.; Scherer, S. W.; Melancon, P. : p200 ARF-GEP1: a Golgi-localized guanine nucleotide exchange protein whose Sec7 domain is targeted b.
- [42799] Further studies establishing the function and utilities of BIG1 are found in John Hopkins OMIM database record ID 604141, and in cited publications numbered 4443-4446 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Channel, Subfamily K, Member 6 (KCNK6, Accession NM_004823) is another VGAM1190 host target gene. KCNK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK6 BINDING SITE, designated SEQ ID:11238, to the

nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42800] Another function of VGAM1190 is therefore inhibition of Potassium Channel, Subfamily K, Member 6 (KCNK6, Accession NM_004823), a gene which is an inward rectifying potassium channel protein. Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK6. The function of KCNK6 has been established by previous studies. Potassium channels perform many distinct functions in both excitable and nonexcitable cells. Members of the tandem pore domain potassium (K2P) channel family, such as TWIK1 (OMIM Ref. No. 601745) and TREK (OMIM Ref. No. 603219), contain 4 transmembrane domains and 2 pore-forming (P) domains. The K2P channels all produce quasi-instantaneous and noninactivating currents but exhibit different types of regulation, indicating that these potassium channels are probably involved in a great diversity of physiologic and pathophysiologic roles (Salinas et al., 1999). Both Chavez et al. (1999) and Pountney et al. (1999) identified cDNAs encoding human KCNK6, which they referred to as TWIK2 and TOSS (TWIK-originated similarity sequence), respectively. Chavez et al. (1999) re-

ported that the predicted 313-amino acid TWIK2 protein shares 54% sequence similarity with TWIK1. Pountney et al. (1999) stated that since TOSS lacks a signal sequence, the N terminus is predicted to be intracellular. They noted that the P2 domain of TOSS contains an unusual GLG motif in a position corresponding to that found in TWIK1. While Chavez et al. (1999) found by Northern blot analysis that the 6.8-, 2.6-, and 1.35-kb TWIK2 mRNAs were expressed in many human tissues, Pountney et al. (1999) reported a more restricted expression pattern. In *Xenopus* oocytes expressing TWIK2, Chavez et al. (1999) detected noninactivating, weak inward rectification, while Pountney et al. (1999) failed to detect any currents above background. By radiation hybrid analysis, Gray et al. (1999) mapped the KCNK6 gene to chromosome 19q13.1.

[42801] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42802] Chavez, R. A.; Gray, A. T.; Zhao, B. B.; Kindler, C. H.; Mazurek, M. J.; Mehta, Y.; Forsayeth, J. R.; Yost, C. S. : TWIK-2, a new weak inward rectifying member of the tandem pore domain potassium channel family. *J. Biol. Chem.* 274: 7887-7892, 1999. ; and

[42803] Gray, A. T.; Kindler, C. H.; Sampson, E. R.; Yost, C. S. : Assignment of KCNK6 encoding the human weak inward rectifier potassium channel TWIK-2 to chromosome band 19q13.1 by radiation.

[42804] Further studies establishing the function and utilities of KCNK6 are found in John Hopkins OMIM database record ID 603939, and in cited publications numbered 5039-5042 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leucine Zipper, Down-regulated In Cancer 1 (LDOC1, Accession NM_012317) is another VGAM1190 host target gene. LDOC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LDOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDOC1 BINDING SITE, designated SEQ ID:14691, to the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42805] Another function of VGAM1190 is therefore inhibition of Leucine Zipper, Down-regulated In Cancer 1 (LDOC1, Accession NM_012317). Accordingly, utilities of VGAM1190

include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDOC1. MGC27382 (Accession NM_144700) is another VGAM1190 host target gene. MGC27382 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC27382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC27382 BINDING SITE, designated SEQ ID:29524, to the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42806] Another function of VGAM1190 is therefore inhibition of MGC27382 (Accession NM_144700). Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC27382. MIG (Accession NM_002416) is another VGAM1190 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, design-

nated SEQ ID:8244, to the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42807] Another function of VGAM1190 is therefore inhibition of MIG (Accession NM_002416). Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. Stromal Cell Derived Factor Receptor 1 (SDFR1, Accession NM_012428) is another VGAM1190 host target gene. SDFR1 BINDING SITE1 and SDFR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SDFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDFR1 BINDING SITE1 and SDFR1 BINDING SITE2, designated SEQ ID:14802 and SEQ ID:18929 respectively, to the nucleotide sequence of VGAM1190 RNA, herein designated VGAM RNA, also designated SEQ ID:3901.

[42808] Another function of VGAM1190 is therefore inhibition of Stromal Cell Derived Factor Receptor 1 (SDFR1, Accession NM_012428). Accordingly, utilities of VGAM1190 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with SDFR1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1191 (VGAM1191) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42809] VGAM1191 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1191 was detected is described hereinabove with reference to Figs. 1–8.

[42810] VGAM1191 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Botrytis Virus F. VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42811] VGAM1191 gene encodes a VGAM1191 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1191 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1191 precursor RNA is designated SEQ ID:1177, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1177 is located at position 5016 relative to the genome of Botrytis Virus F.

- [42812] VGAM1191 precursor RNA folds onto itself, forming VGAM1191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [42813] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1191 folded precursor RNA into VGAM1191 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1191 RNA is designated SEQ ID:3902, and is provided hereinbelow with reference to the sequence listing part.

[42814] VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1191 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42815] VGAM1191 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1191 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1191 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42816] The complementary binding of VGAM1191 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1191 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1191 host target RNA into VGAM1191 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42817] It is appreciated that VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1191 host target genes. The mRNA of each one of this plurality of VGAM1191 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1191 RNA, herein designated VGAM RNA, and which when bound by VGAM1191 RNA causes

inhibition of translation of respective one or more VGAM1191 host target proteins.

[42818] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1191 gene, herein designated VGAM GENE, on one or more VGAM1191 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42819] It is yet further appreciated that a function of VGAM1191 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1191 include diagnosis, prevention and

treatment of viral infection by Botrytis Virus F. Specific functions, and accordingly utilities, of VGAM1191 correlate with, and may be deduced from, the identity of the host target genes which VGAM1191 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42820] Nucleotide sequences of the VGAM1191 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1191 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1191 are further described hereinbelow with reference to Table 1.

[42821] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1191 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1191 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42822] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1191 gene, herein designated VGAM is inhibition of expression of VGAM1191 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1191 correlate with, and may be deduced from, the identity of the target genes which VGAM1191 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42823] Caspase Recruitment Domain Family, Member 15 (CARD15, Accession NM_022162) is a VGAM1191 host target gene. CARD15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD15 BINDING SITE, designated SEQ ID:22715, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42824] A function of VGAM1191 is therefore inhibition of Caspase Recruitment Domain Family, Member 15 (CARD15, Accession NM_022162), a gene which serves as an intracellular receptor for bacterial products in monocytes and transduces signals leading to NFkB activation. Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with CARD15. The function of CARD15 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM126. Huntingtin

(Huntington disease) (HD, Accession NM_002111) is another VGAM1191 host target gene. HD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HD BINDING SITE, designated SEQ ID:7899, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42825] Another function of VGAM1191 is therefore inhibition of Huntingtin (Huntington disease) (HD, Accession NM_002111). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HD. LIM Domain Kinase 1 (LIMK1, Accession NM_016735) is another VGAM1191 host target gene. LIMK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMK1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE, designated SEQ ID:18802, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42826] Another function of VGAM1191 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_016735). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Src Homology Three (SH3) and Cysteine Rich Domain (STAC, Accession NM_003149) is another VGAM1191 host target gene. STAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAC BINDING SITE, designated SEQ ID:9117, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42827] Another function of VGAM1191 is therefore inhibition of Src Homology Three (SH3) and Cysteine Rich Domain

(STAC, Accession NM_003149), a gene which is probably involved in a neuron-specific signal transduction. Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAC. The function of STAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM331. Stromal Interaction Molecule 1 (STIM1, Accession XM_011967) is another VGAM1191 host target gene. STIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STIM1 BINDING SITE, designated SEQ ID:30201, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42828] Another function of VGAM1191 is therefore inhibition of Stromal Interaction Molecule 1 (STIM1, Accession XM_011967), a gene which is very strongly similar to murine Stim1 and may be a transmembrane stromal cell protein. Accordingly, utilities of VGAM1191 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with STIM1. The function of STIM1 has been established by previous studies. Using sequences identified by database searching with a transcript from human chromosome 11p15.5, Parker et al. (1996) screened placental and fetal liver cDNA libraries and cloned a novel cDNA, STIM1, which they called GOK. The deduced 746-amino acid protein contains a predicted signal peptide and transmembrane helix. Parker et al. (1996) also cloned a partial mouse Stim1 genomic clone and found that the human and mouse proteins share 90% sequence identity. Restriction mapping by pulsed field electrophoresis placed the STIM1 gene 1.7 kb telomeric of the RRM1 gene (OMIM Ref. No. 180410) on 11p15.5 (Parker et al., 1996). Sabbioni et al. (1999) determined that the STIM1 gene contains 12 exons that span more than 250 kb between the RRM1 and NUP98 (OMIM Ref. No. 601021) genes.

[42829] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42830] Parker, N. J.; Begley, C. G.; Smith, P. J.; Fox, R. M. : Molecular cloning of a novel human gene (D11S4896E) at chro-

mosomal region 11p15.5. Genomics 37: 253–256, 1996. ;
and

[42831] Sabbioni, S.; Veronese, A.; Trubia, M.; Taramelli, R.; Barbanti-Brodano, G.; Croce, C. M.; Negrini, M. : Exon structure and promoter identification of STIM1 (alias GOK), a human gene ca.

[42832] Further studies establishing the function and utilities of STIM1 are found in John Hopkins OMIM database record ID 605921, and in cited publications numbered 6438–6439 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BMF (Accession NM_033503) is another VGAM1191 host target gene. BMF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BMF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMF BINDING SITE, designated SEQ ID:27283, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42833] Another function of VGAM1191 is therefore inhibition of BMF (Accession NM_033503). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BMF. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_003671) is another VGAM1191 host target gene. CDC14B BINDING SITE1 and CDC14B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDC14B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE1 and CDC14B BINDING SITE2, designated SEQ ID:9760 and SEQ ID:27164 respectively, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42834] Another function of VGAM1191 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_003671). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. MGC12992 (Accession NM_032342) is another VGAM1191 host target gene. MGC12992 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC12992, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12992 BINDING SITE, designated SEQ ID:26136, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42835] Another function of VGAM1191 is therefore inhibition of MGC12992 (Accession NM_032342). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12992. Tripartite Motif-containing 2 (TRIM2, Accession NM_015271) is another VGAM1191 host target gene. TRIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM2 BINDING SITE, designated SEQ ID:17603, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42836] Another function of VGAM1191 is therefore inhibition of Tripartite Motif-containing 2 (TRIM2, Accession NM_015271). Accordingly, utilities of VGAM1191 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM2. LOC92080 (Accession XM_042704) is another VGAM1191 host target gene. LOC92080 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92080, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92080 BINDING SITE, designated SEQ ID:33757, to the nucleotide sequence of VGAM1191 RNA, herein designated VGAM RNA, also designated SEQ ID:3902.

[42837] Another function of VGAM1191 is therefore inhibition of LOC92080 (Accession XM_042704). Accordingly, utilities of VGAM1191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92080. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1192 (VGAM1192) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42838] VGAM1192 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1192 was detected is described hereinabove with reference to Figs. 1-8.

[42839] VGAM1192 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpox Virus. VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42840] VGAM1192 gene encodes a VGAM1192 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1192 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1192 precursor RNA is designated SEQ ID:1178, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1178 is located at position 37365 relative to the genome of Cowpox Virus.

[42841] VGAM1192 precursor RNA folds onto itself, forming VGAM1192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42842] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1192 folded precursor RNA into VGAM1192 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1192 RNA is designated SEQ ID:3903, and is provided hereinbelow with reference to the sequence listing part.

[42843] VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1192 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[42844] VGAM1192 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1192 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1192 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42845] The complementary binding of VGAM1192 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1192 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1192 host target RNA into VGAM1192 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42846] It is appreciated that VGAM1192 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1192 host target genes. The mRNA of each one of this plurality of VGAM1192 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1192 RNA, herein designated VGAM RNA, and which when bound by VGAM1192 RNA causes inhibition of translation of respective one or more VGAM1192 host target proteins.

[42847] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1192 gene, herein designated VGAM GENE, on one or more VGAM1192 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42848] It is yet further appreciated that a function of VGAM1192 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGAM1192 correlate with, and may be deduced from, the identity of the host target genes which VGAM1192 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42849] Nucleotide sequences of the VGAM1192 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1192 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1192 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1192 are further
described hereinbelow with reference to Table 1.

[42850] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1192 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1192 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[42851] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1192 gene, herein designated VGAM is
inhibition of expression of VGAM1192 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1192 correlate with, and may be deduced
from, the identity of the target genes which VGAM1192
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[42852] FLJ12888 (Accession NM_024945) is a VGAM1192 host
target gene. FLJ12888 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ12888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12888 BINDING SITE, designated SEQ ID:24495, to the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, also designated SEQ ID:3903.

[42853] A function of VGAM1192 is therefore inhibition of FLJ12888 (Accession NM_024945). Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12888. FLJ22794 (Accession XM_166220) is another VGAM1192 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44032, to the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, also designated SEQ ID:3903.

[42854] Another function of VGAM1192 is therefore inhibition of

FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. MEP50 (Accession NM_024102) is another VGAM1192 host target gene. MEP50 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEP50, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEP50 BINDING SITE, designated SEQ ID:23547, to the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, also designated SEQ ID:3903.

[42855] Another function of VGAM1192 is therefore inhibition of MEP50 (Accession NM_024102). Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEP50. LOC256846 (Accession XM_170921) is another VGAM1192 host target gene. LOC256846 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC256846 BINDING SITE, designated SEQ ID:45698, to the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, also designated SEQ ID:3903.

[42856] Another function of VGAM1192 is therefore inhibition of LOC256846 (Accession XM_170921). Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256846. LOC90355 (Accession NM_033211) is another VGAM1192 host target gene. LOC90355 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90355 BINDING SITE, designated SEQ ID:27062, to the nucleotide sequence of VGAM1192 RNA, herein designated VGAM RNA, also designated SEQ ID:3903.

[42857] Another function of VGAM1192 is therefore inhibition of LOC90355 (Accession NM_033211). Accordingly, utilities of VGAM1192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90355. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1193 (VGAM1193) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42858] VGAM1193 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1193 was detected is described hereinabove with reference to Figs. 1–8.

[42859] VGAM1193 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42860] VGAM1193 gene encodes a VGAM1193 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1193 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1193 precursor RNA is designated SEQ ID:1179, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1179 is located at position 26098 relative to the genome of Vaccinia Virus.

[42861] VGAM1193 precursor RNA folds onto itself, forming VGAM1193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42862] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1193 folded precursor RNA into VGAM1193 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1193 RNA is designated SEQ ID:3904, and is provided hereinbelow with reference to the sequence listing part.

[42863] VGAM1193 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1193 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42864] VGAM1193 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1193 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1193 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1193 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[42865] The complementary binding of VGAM1193 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1193 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1193 host target RNA into VGAM1193 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42866] It is appreciated that VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1193 host target genes. The mRNA of each one of this plurality of VGAM1193 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1193 RNA, herein designated VGAM RNA, and which when bound by VGAM1193 RNA causes inhibition of translation of respective one or more

VGAM1193 host target proteins.

[42867] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1193 gene, herein designated VGAM GENE, on one or more VGAM1193 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42868] It is yet further appreciated that a function of VGAM1193 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1193 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific

functions, and accordingly utilities, of VGAM1193 correlate with, and may be deduced from, the identity of the host target genes which VGAM1193 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42869] Nucleotide sequences of the VGAM1193 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1193 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1193 are further described hereinbelow with reference to Table 1.

[42870] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1193 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1193 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42871] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1193 gene, herein designated VGAM is inhibition of expression of VGAM1193 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1193 correlate with, and may be deduced from, the identity of the target genes which VGAM1193 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42872] Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM_003038) is a VGAM1193 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:8997, to the nucleotide sequence of VGAM1193 RNA, herein designated VGAM RNA, also designated SEQ ID:3904.

[42873] A function of VGAM1193 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM_003038), a gene which transports alanine, serine, cysteine, and threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM859.BC008967 (Accession XM_027309) is another VGAM1193 host target gene. BC008967 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BC008967, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BC008967 BINDING SITE, designated SEQ ID:30476, to the nucleotide sequence of VGAM1193 RNA, herein designated VGAM RNA, also designated SEQ ID:3904.

[42874] Another function of VGAM1193 is therefore inhibition of BC008967 (Accession XM_027309). Accordingly, utilities of VGAM1193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BC008967. LOC158722 (Accession XM_088653) is another VGAM1193 host target gene. LOC158722 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC158722 BINDING SITE, designated SEQ ID:39889, to the nucleotide sequence of VGAM1193 RNA, herein designated VGAM RNA, also designated SEQ ID:3904.

[42875] Another function of VGAM1193 is therefore inhibition of LOC158722 (Accession XM_088653). Accordingly, utilities of VGAM1193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158722. LOC91650 (Accession XM_039853) is another VGAM1193 host target gene. LOC91650 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91650 BINDING SITE, designated SEQ ID:33200, to the nucleotide sequence of VGAM1193 RNA, herein designated VGAM RNA, also designated SEQ ID:3904.

[42876] Another function of VGAM1193 is therefore inhibition of LOC91650 (Accession XM_039853). Accordingly, utilities of VGAM1193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91650. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1194 (VGAM1194) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42877] VGAM1194 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1194 was detected is described hereinabove with reference to Figs. 1–8.

[42878] VGAM1194 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42879] VGAM1194 gene encodes a VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1194 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1194 precursor RNA is designated SEQ ID:1180, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1180 is located at position 25686 relative to the

genome of Camelpox Virus.

[42880] VGAM1194 precursor RNA folds onto itself, forming VGAM1194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42881] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1194 folded precursor RNA into VGAM1194 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1194 RNA is designated SEQ ID:3905, and is provided hereinbelow with reference to the sequence listing part.

[42882] VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1194 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42883] VGAM1194 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1194 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1194 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42884] The complementary binding of VGAM1194 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1194 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1194 host target RNA into VGAM1194 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42885] It is appreciated that VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1194 host target genes. The mRNA of each one of this plurality of VGAM1194 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1194 RNA, herein designated VGAM RNA, and which when bound by VGAM1194 RNA causes inhibition of translation of respective one or more VGAM1194 host target proteins.

[42886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1194 gene, herein designated VGAM GENE, on one or more VGAM1194 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42887] It is yet further appreciated that a function of VGAM1194 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1194 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1194 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42888] Nucleotide sequences of the VGAM1194 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1194 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1194 are further described hereinbelow with reference to Table 1.

[42889] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1194 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1194 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42890] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1194 gene, herein designated VGAM is inhibition of expression of VGAM1194 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1194 correlate with, and may be deduced

from, the identity of the target genes which VGAM1194 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42891] Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM_001399) is a VGAM1194 host target gene. ED1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ED1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ED1 BINDING SITE, designated SEQ ID:7101, to the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, also designated SEQ ID:3905.

[42892] A function of VGAM1194 is therefore inhibition of Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM_001399). Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ED1. Oxidative-stress Responsive 1 (OSR1, Accession NM_005109) is another VGAM1194 host target gene. OSR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSR1 BINDING SITE, designated SEQ ID:11590, to the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, also designated SEQ ID:3905.

[42893] Another function of VGAM1194 is therefore inhibition of Oxidative-stress Responsive 1 (OSR1, Accession NM_005109), a gene which mediates stress-activated signals. Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSR1. The function of OSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM_138325) is another VGAM1194 host target gene. PACE4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PACE4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE4 BINDING SITE, designated SEQ ID:28726, to the nucleotide sequence of VGAM1194 RNA,

herein designated VGAM RNA, also designated SEQ ID:3905.

[42894] Another function of VGAM1194 is therefore inhibition of Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM_138325), a gene which processes hormone precursors by cleaving paired basic amino acids. Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE4. The function of PACE4 has been established by previous studies. Using PCR methods, Kiefer et al. (1991) identified a second human subtilisin-like protease gene on chromosome 15. PCR primers were designed to be specific for the subfamily of eukaryotic subtilisin-like proteases with specificity for paired basic amino acid residue processing motifs. The gene encoding this protease, designated PACE4, also encoded a smaller subtilisin-related polypeptide derived by alternative mRNA splicing. As with the product of the PACE gene (OMIM Ref. No. 136950), the tissue distribution of PACE4 was widespread, with comparatively higher levels in the liver. By in situ hybridization using isolated cosmid clones, Kiefer et al. (1991) mapped the PACE4 gene to chromosome 15 in close proximity to the PACE gene at

15q25–q26. Double labeling in situ hybridization suggested that the 2 genes are within 5 megabases of each other. Mbikay et al. (1995) mapped the gene for PACE4 (Pcsk6) to mouse chromosome 7 by RFLP analysis of a DNA panel from an interspecific backcross. It was located at a distance of 13 cM from the Pcsk3 locus, which specifies furin (OMIM Ref. No. 136950), another member of this family of enzymes previously mapped to mouse chromosome 7. This is in concordance with the known close proximity of these 2 loci in the homologous region on human 15q25–qter. Pcsk3 and Pcsk6 map to a region of mouse chromosome 7 that has been associated cytogenetically with postnatal lethality in maternal disomy, suggesting that these genes may be imprinted.

[42895] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42896] Kiefer, M. C.; Tucker, J. E.; Joh, R.; Landsberg, K. E.; Saltman, D.; Barr, P. J. : Identification of a second human subtilisin-like protease gene in the fes/fps region of chromosome 15. DNA Cell Biol. 10: 757–769, 1991. ; and

[42897] Mbikay, M.; Seidah, N. G.; Chretien, M.; Simpson, E. M. : Chromosomal assignment of the genes for proprotein

convertases PC4, PC5, and PACE 4 in mouse and human. Genomics 26: 123–129, 19.

[42898] Further studies establishing the function and utilities of PACE4 are found in John Hopkins OMIM database record ID 167405, and in cited publications numbered 10330 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1462 (Accession XM_166132) is another VGAM1194 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43921, to the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, also designated SEQ ID:3905.

[42899] Another function of VGAM1194 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. LOC145945 (Accession XM_096908) is another VGAM1194 host target gene. LOC145945 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40636, to the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, also designated SEQ ID:3905.

[42900] Another function of VGAM1194 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC219401 (Accession XM_166706) is another VGAM1194 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44595, to the nucleotide sequence of VGAM1194 RNA, herein designated VGAM RNA, also designated SEQ ID:3905.

[42901] Another function of VGAM1194 is therefore inhibition of

LOC219401 (Accession XM_166706). Accordingly, utilities of VGAM1194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1195 (VGAM1195) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42902] VGAM1195 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1195 was detected is described hereinabove with reference to Figs. 1-8.

[42903] VGAM1195 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42904] VGAM1195 gene encodes a VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1195 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1195 precursor RNA is designated SEQ ID:1181, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1181 is located at position 79725 relative to the genome of Equine Herpesvirus 1.

- [42905] VGAM1195 precursor RNA folds onto itself, forming VGAM1195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [42906] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1195 folded precursor RNA into VGAM1195 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1195 RNA is designated SEQ ID:3906, and is provided hereinbelow with reference to the sequence listing part.

[42907] VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1195 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42908] VGAM1195 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1195 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1195 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[42909] The complementary binding of VGAM1195 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1195 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1195 host target RNA into VGAM1195 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42910] It is appreciated that VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1195 host target genes. The mRNA of each one of this plurality of VGAM1195 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1195 RNA, herein designated VGAM RNA, and which when bound by VGAM1195 RNA causes inhibition of translation of respective one or more VGAM1195 host target proteins.

[42911] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1195 gene, herein designated VGAM GENE, on one or more VGAM1195 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42912] It is yet further appreciated that a function of VGAM1195

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1195 correlate with, and may be deduced from, the identity of the host target genes which VGAM1195 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42913] Nucleotide sequences of the VGAM1195 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1195 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1195 are further described hereinbelow with reference to Table 1.

[42914] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1195 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1195 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42915] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1195 gene, herein designated VGAM is inhibition of expression of VGAM1195 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1195 correlate with, and may be deduced from, the identity of the target genes which VGAM1195 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42916] Dihydrofolate Reductase (DHFR, Accession NM_000791) is a VGAM1195 host target gene. DHFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHFR BINDING SITE, designated SEQ ID:6445, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42917] A function of VGAM1195 is therefore inhibition of Dihydrofolate Reductase (DHFR, Accession NM_000791), a gene which converts dihydrofolate into tetrahydrofolate. Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with DHFR. The function of DHFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM826.Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_005231) is another VGAM1195 host target gene. EMS1 BINDING SITE1 and EMS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EMS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMS1 BINDING SITE1 and EMS1 BINDING SITE2, designated SEQ ID:11734 and SEQ ID:28865 respectively, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42918] Another function of VGAM1195 is therefore inhibition of Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_005231), a gene which may contribute to the organization of cell structure. in transformed cells may contribute to cellular growth regulation and transformation.

Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMS1. The function of EMS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497. Transcription Factor CP2 (TFCP2, Accession NM_005653) is another VGAM1195 host target gene. TFCP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TFCP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFCP2 BINDING SITE, designated SEQ ID:12192, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42919] Another function of VGAM1195 is therefore inhibition of Transcription Factor CP2 (TFCP2, Accession NM_005653), a gene which is a transcription factor CP2 and recognizes sites within the alpha-globin gene and SV40 late promoters. Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFCP2. The function of TFCP2 has

been established by previous studies. Lambert et al. (2000) reported an association between a noncoding polymorphism (G-A) in the 3-prime untranslated region of TFCP2 and sporadic Alzheimer disease (AD5; 602096) in French and British populations and a similar trend in a North American population. The combined analysis of the 3 independent populations suggested a protective effect of the A allele (OR = 0.58, 95% CI 0.44–0.75). The A allele demonstrated reduced binding to nuclear protein(s) from a neuroblastoma cell line, and absence of the A allele was associated with lower gene expression in lymphocytes from AD cases compared with controls. The authors suggested that polymorphic variation in TFCP2 may be important for the pathogenesis of AD, particularly since the gene product interacts with proteins such as GSK3B (OMIM Ref. No. 605004), Fe65 (OMIM Ref. No. 602709), and certain factors involved in the inflammatory response. Swendeman et al. (1994) characterized the genomic structure, chromosome location, promoter, and expression pattern of CP2, a 66-kD cellular transcription factor that interacts with the alpha-globin (OMIM Ref. No. 141800) promoter as well as with additional cellular and viral promoter elements. Homodimers of CP2, together with a 45-kD part-

ner protein, form the so-called stage selector protein complex (Jane et al., 1995) that binds to a proximal gamma-globin gene promoter regulatory sequence, termed the stage selector element (SSE). The SSE is thought to be involved in silencing beta globin gene (OMIM Ref. No. 141900) transcription during fetal erythropoiesis (Cunningham et al., 1995).

[42920] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[42921] Swendeman, S. L.; Spielholz, C.; Jenkins, N. A.; Gilbert, D. J.; Copeland, N. G.; Sheffery, M. : Characterization of the genomic structure, chromosomal location, promoter, and developmental expression of the alpha-globin transcription factor CP2. J. Biol. Chem. 269: 11663–11671, 1994. ; and

[42922] Lambert, J.-C.; Goumidi, L.; Wavrant-De Vrieze, F.; Frigard, B.; Harris, J. M.; Cummings, A.; Coates, J.; Pasquier, F.; Cotel, D.; Gaillac, M.; St. Clair, D.; Mann, D. M. A.; Hardy, J.;

[42923] Further studies establishing the function and utilities of TFCEP2 are found in John Hopkins OMIM database record ID 189889, and in cited publications numbered

12343–1234 and 12346–12348 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Wolf–Hirschhorn Syndrome Candidate 1–like 1 (WHSC1L1, Accession NM_017778) is another VGAM1195 host target gene. WHSC1L1 BINDING SITE1 and WHSC1L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1L1 BINDING SITE1 and WHSC1L1 BINDING SITE2, designated SEQ ID:19408 and SEQ ID:23315 respectively, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42924] Another function of VGAM1195 is therefore inhibition of Wolf–Hirschhorn Syndrome Candidate 1–like 1 (WHSC1L1, Accession NM_017778), a gene which restores repair of base–base and single– nucleotide insertion–deletion mismatches, and increases the proficiency to process heteroduplexes with insertion–deletion mismatches. Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associ–

ated with WHSC1L1. The function of WHSC1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM475. KIAA1922 (Accession XM_057040) is another VGAM1195 host target gene.

KIAA1922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1922 BINDING SITE, designated SEQ ID:36458, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42925] Another function of VGAM1195 is therefore inhibition of KIAA1922 (Accession XM_057040). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1922. Ring Finger Protein 24 (RNF24, Accession NM_007219) is another VGAM1195 host target gene. RNF24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF24, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF24 BINDING SITE, designated SEQ ID:14089, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42926] Another function of VGAM1195 is therefore inhibition of Ring Finger Protein 24 (RNF24, Accession NM_007219). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF24. SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession NM_003003) is another VGAM1195 host target gene. SEC14L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC14L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC14L1 BINDING SITE, designated SEQ ID:8899, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42927] Another function of VGAM1195 is therefore inhibition of SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession

NM_003003). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC14L1. Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869) is another VGAM1195 host target gene. SEZ6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEZ6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEZ6 BINDING SITE, designated SEQ ID:36770, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42928] Another function of VGAM1195 is therefore inhibition of Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEZ6. WSB1 (Accession NM_134264) is another VGAM1195 host target gene. WSB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WSB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of WSB1 BINDING SITE, designated SEQ ID:28613, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42929] Another function of VGAM1195 is therefore inhibition of WSB1 (Accession NM_134264). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WSB1. LOC150183 (Accession XM_097839) is another VGAM1195 host target gene. LOC150183 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150183 BINDING SITE, designated SEQ ID:41153, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42930] Another function of VGAM1195 is therefore inhibition of LOC150183 (Accession XM_097839). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150183. LOC150184 (Accession XM_097840) is an-

other VGAM1195 host target gene. LOC150184 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150184 BINDING SITE, designated SEQ ID:41154, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42931] Another function of VGAM1195 is therefore inhibition of LOC150184 (Accession XM_097840). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150184. LOC150185 (Accession XM_097834) is another VGAM1195 host target gene. LOC150185 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150185 BINDING SITE, designated SEQ ID:41150, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42932] Another function of VGAM1195 is therefore inhibition of LOC150185 (Accession XM_097834). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150185. LOC255654 (Accession XM_173036) is another VGAM1195 host target gene. LOC255654 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255654 BINDING SITE, designated SEQ ID:46300, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42933] Another function of VGAM1195 is therefore inhibition of LOC255654 (Accession XM_173036). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255654. LOC91069 (Accession XM_035824) is another VGAM1195 host target gene. LOC91069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91069, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91069 BINDING SITE, designated SEQ ID:32343, to the nucleotide sequence of VGAM1195 RNA, herein designated VGAM RNA, also designated SEQ ID:3906.

[42934] Another function of VGAM1195 is therefore inhibition of LOC91069 (Accession XM_035824). Accordingly, utilities of VGAM1195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91069. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1196 (VGAM1196) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42935] VGAM1196 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1196 was detected is described hereinabove with reference to Figs. 1-8.

[42936] VGAM1196 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1196 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[42937] VGAM1196 gene encodes a VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1196 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1196 precursor RNA is designated SEQ ID:1182, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1182 is located at position 82687 relative to the genome of Equine Herpesvirus 1.

[42938] VGAM1196 precursor RNA folds onto itself, forming VGAM1196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42939] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1196 folded precursor RNA into VGAM1196

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1196 RNA is designated SEQ ID:3907, and is provided hereinbelow with reference to the sequence listing part.

[42940] VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1196 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42941] VGAM1196 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1196 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1196 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42942] The complementary binding of VGAM1196 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1196 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1196 host target RNA into VGAM1196 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[42943] It is appreciated that VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1196 host target genes. The mRNA of each one of this plurality of VGAM1196 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1196 RNA, herein designated VGAM RNA, and which when bound by VGAM1196 RNA causes inhibition of translation of respective one or more VGAM1196 host target proteins.

[42944] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1196 gene, herein designated VGAM GENE, on one or more VGAM1196 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42945] It is yet further appreciated that a function of VGAM1196 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1196 correlate with, and may be deduced from, the identity of the host target genes which VGAM1196 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42946] Nucleotide sequences of the VGAM1196 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1196 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1196 are further described hereinbelow with reference to Table 1.

[42947] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1196 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1196 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42948] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1196 gene, herein designated VGAM is inhibition of expression of VGAM1196 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1196 correlate with, and may be deduced from, the identity of the target genes which VGAM1196 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42949] Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718) is a VGAM1196 host target gene. BMP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BMP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP6 BINDING SITE, designated SEQ ID:7455, to the nucleotide sequence of VGAM1196 RNA, herein designated

VGAM RNA, also designated SEQ ID:3907.

[42950] A function of VGAM1196 is therefore inhibition of Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718), a gene which induces cartilage and bone formation. Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP6. The function of BMP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233. Chromosome 20 Open Reading Frame 18 (C20orf18, Accession NM_031228) is another VGAM1196 host target gene. C20orf18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf18 BINDING SITE, designated SEQ ID:25277, to the nucleotide sequence of VGAM1196 RNA, herein designated VGAM RNA, also designated SEQ ID:3907.

[42951] Another function of VGAM1196 is therefore inhibition of Chromosome 20 Open Reading Frame 18 (C20orf18, Ac-

cession NM_031228). Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf18.

FLJ10921 (Accession NM_018272) is another VGAM1196 host target gene. FLJ10921 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10921, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10921 BINDING SITE, designated SEQ ID:20250, to the nucleotide sequence of VGAM1196 RNA, herein designated VGAM RNA, also designated SEQ ID:3907.

[42952] Another function of VGAM1196 is therefore inhibition of FLJ10921 (Accession NM_018272). Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10921. LOC220038 (Accession XM_166257) is another VGAM1196 host target gene. LOC220038 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC220038 BINDING SITE, designated SEQ ID:44082, to the nucleotide sequence of VGAM1196 RNA, herein designated VGAM RNA, also designated SEQ ID:3907.

[42953] Another function of VGAM1196 is therefore inhibition of LOC220038 (Accession XM_166257). Accordingly, utilities of VGAM1196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220038. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1197 (VGAM1197) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42954] VGAM1197 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1197 was detected is described hereinabove with reference to Figs. 1–8.

[42955] VGAM1197 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[42956] VGAM1197 gene encodes a VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1197 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1197 precursor RNA is designated SEQ ID:1183, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1183 is located at position 80050 relative to the genome of Equine Herpesvirus 1.

[42957] VGAM1197 precursor RNA folds onto itself, forming VGAM1197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[42958] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1197 folded precursor RNA into VGAM1197 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1197 RNA is designated SEQ ID:3908, and is provided hereinbelow with reference to the sequence listing part.

[42959] VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1197 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42960] VGAM1197 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1197 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1197 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42961] The complementary binding of VGAM1197 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1197 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1197 host target RNA into VGAM1197 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42962] It is appreciated that VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1197 host target genes. The mRNA of each one of this plurality of VGAM1197 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1197 RNA, herein designated VGAM RNA, and which when bound by VGAM1197 RNA causes inhibition of translation of respective one or more VGAM1197 host target proteins.

[42963] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1197 gene, herein designated VGAM GENE, on one or more VGAM1197 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42964] It is yet further appreciated that a function of VGAM1197 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1197 correlate with, and may be deduced from, the identity of the host target genes which VGAM1197 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42965] Nucleotide sequences of the VGAM1197 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1197 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1197 are further described hereinbelow with reference to Table 1.

[42966] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1197 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1197 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42967] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1197 gene, herein designated VGAM is inhibition of expression of VGAM1197 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1197 correlate with, and may be deduced from, the identity of the target genes which VGAM1197 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42968] Deleted In Azoospermia-like (DAZL, Accession XM_042839) is a VGAM1197 host target gene. DAZL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAZL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAZL BINDING SITE, designated SEQ ID:33799, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42969] A function of VGAM1197 is therefore inhibition of Deleted In Azoospermia-like (DAZL, Accession XM_042839), a gene which may be essential for gametogenesis. Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAZL. The function of DAZL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Fanconi Anemia, Complementation Group G (FANCG, Accession NM_004629) is another VGAM1197 host target gene. FANCG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FANCG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCG BINDING SITE, designated SEQ ID:11000, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42970] Another function of VGAM1197 is therefore inhibition of Fanconi Anemia, Complementation Group G (FANCG, Accession NM_004629). Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with FANCG. Regenerating Islet-derived 1 Alpha (pancreatic stone protein, pancreatic thread protein) (REG1A, Accession XM_114278) is another VGAM1197 host target gene. REG1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by REG1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REG1A BINDING SITE, designated SEQ ID:42827, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42971] Another function of VGAM1197 is therefore inhibition of Regenerating Islet-derived 1 Alpha (pancreatic stone protein, pancreatic thread protein) (REG1A, Accession XM_114278), a gene which plays an important role in exocrine pancreatic function, and inhibits CaCO₃ crystal growth. Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REG1A. The function of REG1A has been established by previous studies. Pancreatic stone protein is the major component of the protein matrix of calculi in patients suffering from chronic calcifying pan-

creatitis. Secretory pancreatic stone protein is a glycoprotein in the pancreatic secretion. This protein, called PSPS, occurs in multiple molecular forms due to posttranslational processing. The abundance of PSPS in pancreatic juice (10 to 14% of total protein) suggests that it plays an important role in exocrine pancreatic function. In vitro experiments show that PSPS inhibits CaCO_3 crystal growth. Since in all the pancreatic secretions are supersaturated in calcium carbonate, the physiologic role of PSPS may be related to its inhibitory properties. Demonstration of diminished PSPS in the pancreatic juice of patients with chronic calcifying pancreatitis supported that hypothesis. Giorgi et al. (1989) isolated a cDNA encoding pre-PSPS from a human pancreatic cDNA library. They found that PSPS mRNA was 3 times lower in chronic calcifying pancreatitis than in controls; the message for trypsinogen, chymotrypsinogen, and colipase were not altered. Giorgi et al. (1989) concluded that PSPS gene expression is specifically reduced in CCP patients. Is a defect in this gene the basis for some cases of hereditary pancreatitis (OMIM Ref. No. 167800)? Terazono et al. (1988) cloned and sequenced a cDNA derived from pancreatic islets following partial pancreatectomy. On the basis of its induction during regrowth of the

pancreas and its apparent origin from islets, the corresponding gene was termed REG (for regeneration) with the implication that the gene was involved in islet regeneration. Stewart (1989) found that the sequence was identical to that of pancreatic stone protein. Verdier et al. (1992), who referred to pancreatic stone protein as lithostathine (Sarles et al., 1990), presented evidence that the kidney produces a protein immunologically similar to lithostathine. They suggested that it is responsible for preventing the formation of renal stones since the urine in the thin descending limb of the Henle loop is supersaturated in CaCO_3 as is pancreatic juice. Akiyama et al. (2001) studied the mechanism by which the REG gene is activated in beta cells. They found that the combined addition of interleukin-6 (OMIM Ref. No. 147620) and dexamethasone induced the expression of the REG gene in beta cells and that inhibitors of poly(ADP-ribose) polymerase (PARP; 173870) enhanced the expression. PARP inhibitors enhanced the DNA-protein complex formation for REG gene transcription and stabilized the complex by inhibiting the autopoly(ADP-ribosylation) of PARP.

[42972] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [42973] Sarles, H.; Dagorn, J. C.; Giorgi, D.; Bernard, J. P. : Renaming pancreatic stone protein as 'lithostathine'. (Letter) Gastroenterology 99: 900–901, 1990. ; and
- [42974] Akiyama, T.; Takasawa, S.; Nata, K.; Kobayashi, S.; Abe, M.; Shervani, N. J.; Ikeda, T.; Nakagawa, K.; Unno, M.; Matsuno, S.; Okamoto, H. : Activation of Reg gene, a gene for insulin-pr.
- [42975] Further studies establishing the function and utilities of REG1A are found in John Hopkins OMIM database record ID 167770, and in cited publications numbered 10918–1091 and 10919–10924 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sex Comb On Midleg-like 1 (Drosophila) (SCML1, Accession NM_006746) is another VGAM1197 host target gene. SCML1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCML1 BINDING SITE, designated SEQ ID:13592, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3908.

[42976] Another function of VGAM1197 is therefore inhibition of Sex Comb On Midleg-like 1 (Drosophila) (SCML1, Accession NM_006746). Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCML1. BANK (Accession NM_017935) is another VGAM1197 host target gene. BANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANK BINDING SITE, designated SEQ ID:19625, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42977] Another function of VGAM1197 is therefore inhibition of BANK (Accession NM_017935). Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANK. KIAA0553 (Accession XM_045981) is another VGAM1197 host target gene. KIAA0553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0553, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0553 BINDING SITE, designated SEQ ID:34632, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42978] Another function of VGAM1197 is therefore inhibition of KIAA0553 (Accession XM_045981). Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0553. PRO0097 (Accession NM_014114) is another VGAM1197 host target gene. PRO0097 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0097 BINDING SITE, designated SEQ ID:15363, to the nucleotide sequence of VGAM1197 RNA, herein designated VGAM RNA, also designated SEQ ID:3908.

[42979] Another function of VGAM1197 is therefore inhibition of PRO0097 (Accession NM_014114). Accordingly, utilities of VGAM1197 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRO0097. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1198 (VGAM1198) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[42980] VGAM1198 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1198 was detected is described hereinabove with reference to Figs. 1–8.

[42981] VGAM1198 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 1. VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[42982] VGAM1198 gene encodes a VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1198 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1198 precursor RNA is desig-

nated SEQ ID:1184, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1184 is located at position 80155 relative to the genome of Equine Herpesvirus 1.

- [42983] VGAM1198 precursor RNA folds onto itself, forming VGAM1198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [42984] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1198 folded precursor RNA into VGAM1198 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1198 RNA is designated SEQ ID:3909, and is provided hereinbelow with reference to the sequence

listing part.

[42985] VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1198 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[42986] VGAM1198 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1198 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1198 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[42987] The complementary binding of VGAM1198 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1198 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1198 host target RNA into VGAM1198 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[42988] It is appreciated that VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1198 host target genes. The mRNA of each one of this plurality of VGAM1198 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1198 RNA, herein designated VGAM

RNA, and which when bound by VGAM1198 RNA causes inhibition of translation of respective one or more VGAM1198 host target proteins.

[42989] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1198 gene, herein designated VGAM GENE, on one or more VGAM1198 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[42990] It is yet further appreciated that a function of VGAM1198 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1198 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1198 correlate with, and may be deduced from, the identity of the host target genes which VGAM1198 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[42991] Nucleotide sequences of the VGAM1198 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1198 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1198 are further described hereinbelow with reference to Table 1.

[42992] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1198 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1198 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[42993] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1198 gene, herein designated VGAM is

inhibition of expression of VGAM1198 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1198 correlate with, and may be deduced from, the identity of the target genes which VGAM1198 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[42994] Polymerase (DNA directed), Eta (POLH, Accession NM_006502) is a VGAM1198 host target gene. POLH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by POLH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLH BINDING SITE, designated SEQ ID:13248, to the nucleotide sequence of VGAM1198 RNA, herein designated VGAM RNA, also designated SEQ ID:3909.

[42995] A function of VGAM1198 is therefore inhibition of Polymerase (DNA directed), Eta (POLH, Accession NM_006502). Accordingly, utilities of VGAM1198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLH. N-myristoyltransferase 1 (NMT1, Accession NM_021079) is another VGAM1198 host target gene. NMT1 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NMT1 BINDING SITE, designated SEQ ID:22047, to the nucleotide sequence of VGAM1198 RNA, herein designated VGAM RNA, also designated SEQ ID:3909.

[42996] Another function of VGAM1198 is therefore inhibition of N-myristoyltransferase 1 (NMT1, Accession NM_021079). Accordingly, utilities of VGAM1198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NMT1. LOC150208 (Accession XM_097841) is another VGAM1198 host target gene. LOC150208 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150208, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150208 BINDING SITE, designated SEQ ID:41157, to the nucleotide sequence of VGAM1198 RNA, herein designated VGAM RNA, also designated SEQ ID:3909.

[42997] Another function of VGAM1198 is therefore inhibition of LOC150208 (Accession XM_097841). Accordingly, utilities of VGAM1198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150208. LOC255631 (Accession XM_171267) is another VGAM1198 host target gene. LOC255631 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255631, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255631 BINDING SITE, designated SEQ ID:46039, to the nucleotide sequence of VGAM1198 RNA, herein designated VGAM RNA, also designated SEQ ID:3909.

[42998] Another function of VGAM1198 is therefore inhibition of LOC255631 (Accession XM_171267). Accordingly, utilities of VGAM1198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255631. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1199 (VGAM1199) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[42999] VGAM1199 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1199 was detected is described hereinabove with reference to Figs. 1-8.

[43000] VGAM1199 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Nephritis Virus. VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43001] VGAM1199 gene encodes a VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1199 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1199 precursor RNA is designated SEQ ID:1185, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1185 is located at position 6153 relative to the genome of Avian Nephritis Virus.

[43002] VGAM1199 precursor RNA folds onto itself, forming VGAM1199 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43003] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1199 folded precursor RNA into VGAM1199 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1199 RNA is designated SEQ ID:3910, and is provided hereinbelow with reference to the sequence listing part.

[43004] VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1199 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43005] VGAM1199 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1199 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1199 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43006] The complementary binding of VGAM1199 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1199 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1199 host target RNA into VGAM1199 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43007] It is appreciated that VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1199 host target genes. The mRNA of each one of this plurality of VGAM1199 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1199 RNA, herein designated VGAM RNA, and which when bound by VGAM1199 RNA causes inhibition of translation of respective one or more VGAM1199 host target proteins.

[43008] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1199 gene, herein designated VGAM GENE, on one or more VGAM1199 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43009] It is yet further appreciated that a function of VGAM1199 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1199 include diagnosis, prevention and treatment of viral infection by Avian Nephritis Virus. Specific functions, and accordingly utilities, of VGAM1199 correlate with, and may be deduced from, the identity of the host target genes which VGAM1199 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[43010] Nucleotide sequences of the VGAM1199 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1199 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1199 are further described hereinbelow with reference to Table 1.

[43011] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1199 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1199 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43012] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1199 gene, herein designated VGAM is inhibition of expression of VGAM1199 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1199 correlate with, and may be deduced from, the identity of the target genes which VGAM1199 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43013] CD164 Antigen, Sialomucin (CD164, Accession NM_006016) is a VGAM1199 host target gene. CD164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD164 BINDING SITE, designated SEQ ID:12628, to the nucleotide sequence of VGAM1199 RNA, herein designated VGAM RNA, also designated SEQ ID:3910.

[43014] A function of VGAM1199 is therefore inhibition of CD164 Antigen, Sialomucin (CD164, Accession NM_006016), a gene which plays a role in hematopoiesis by facilitating the adhesion of CD34+ cells to bone marrow stroma and negatively regulates CD34+ hematopoietic progenitor cell growth. Accordingly, utilities of VGAM1199 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD164. The function of CD164 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM75.LOC157226 (Accession XM_033876) is another VGAM1199 host target gene. LOC157226 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157226 BINDING SITE, designated SEQ ID:31974, to the nucleotide sequence of VGAM1199 RNA, herein designated VGAM RNA, also designated SEQ ID:3910.

[43015] Another function of VGAM1199 is therefore inhibition of LOC157226 (Accession XM_033876). Accordingly, utilities of VGAM1199 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157226. LOC91974 (Accession XM_041974) is another VGAM1199 host target gene. LOC91974 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91974, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91974 BINDING SITE, designated SEQ ID:33650, to the nucleotide sequence of VGAM1199 RNA, herein designated VGAM RNA, also designated SEQ ID:3910.

[43016] Another function of VGAM1199 is therefore inhibition of

LOC91974 (Accession XM_041974). Accordingly, utilities of VGAM1199 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91974. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1200 (VGAM1200) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43017] VGAM1200 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1200 was detected is described hereinabove with reference to Figs. 1-8.

[43018] VGAM1200 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Nephritis Virus. VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43019] VGAM1200 gene encodes a VGAM1200 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1200 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1200 precursor RNA is designated SEQ ID:1186, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1186 is located at position 5356 relative to the genome of Avian Nephritis Virus.

[43020] VGAM1200 precursor RNA folds onto itself, forming VGAM1200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43021] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1200 folded precursor RNA into VGAM1200 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide se-

quence of VGAM1200 RNA is designated SEQ ID:3911, and is provided hereinbelow with reference to the sequence listing part.

[43022] VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1200 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43023] VGAM1200 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1200 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1200 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[43024] The complementary binding of VGAM1200 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1200 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1200 host target RNA into VGAM1200 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43025] It is appreciated that VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1200 host target genes. The mRNA of each one of this plurality of VGAM1200 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1200 RNA, herein designated VGAM RNA, and which when bound by VGAM1200 RNA causes inhibition of translation of respective one or more VGAM1200 host target proteins.

[43026] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1200 gene, herein designated VGAM GENE, on one or more VGAM1200 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43027] It is yet further appreciated that a function of VGAM1200

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of viral infection by Avian Nephritis Virus. Specific functions, and accordingly utilities, of VGAM1200 correlate with, and may be deduced from, the identity of the host target genes which VGAM1200 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43028] Nucleotide sequences of the VGAM1200 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1200 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1200 are further described hereinbelow with reference to Table 1.

[43029] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1200 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1200 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43030] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1200 gene, herein designated VGAM is inhibition of expression of VGAM1200 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1200 correlate with, and may be deduced from, the identity of the target genes which VGAM1200 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43031] Adenylate Cyclase 6 (ADCY6, Accession NM_015270) is a VGAM1200 host target gene. ADCY6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADCY6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE, designated SEQ ID:17590, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43032] A function of VGAM1200 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM_015270), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ADCY6. The function of ADCY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM22. Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692) is another VGAM1200 host target gene. ALDH1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH1B1 BINDING SITE, designated SEQ ID:6349, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43033] Another function of VGAM1200 is therefore inhibition of Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH1B1. Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434) is another VGAM1200 host target gene. DAAM2 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44327, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43034] Another function of VGAM1200 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAAM2. The function of DAAM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is another VGAM1200 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7742, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43035] Another function of VGAM1200 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Growth Arrest-specific 7 (GAS7, Accession NM_003644) is another VGAM1200 host target gene. GAS7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAS7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS7 BINDING SITE, designated SEQ ID:9713, to the nucleotide sequence of VGAM1200 RNA, herein

designated VGAM RNA, also designated SEQ ID:3911.

[43036] Another function of VGAM1200 is therefore inhibition of Growth Arrest-specific 7 (GAS7, Accession NM_003644), a gene which may play a role in promoting maturation and morphological differentiation of cerebellar neurons. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS7. The function of GAS7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. Keratocan (KERA, Accession NM_007035) is another VGAM1200 host target gene. KERA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KERA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KERA BINDING SITE, designated SEQ ID:13909, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43037] Another function of VGAM1200 is therefore inhibition of Keratocan (KERA, Accession NM_007035), a gene which may be important in developing and maintaining corneal

transparency and for the structure of the stromal matrix. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KERA. The function of KERA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM723. Matrix Metalloproteinase 25 (MMP25, Accession NM_022468) is another VGAM1200 host target gene. MMP25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP25 BINDING SITE, designated SEQ ID:22820, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43038] Another function of VGAM1200 is therefore inhibition of Matrix Metalloproteinase 25 (MMP25, Accession NM_022468). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP25. Periplakin (PPL, Accession NM_002705) is another VGAM1200 host target

gene. PPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPL BINDING SITE, designated SEQ ID:8553, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43039] Another function of VGAM1200 is therefore inhibition of Periplakin (PPL, Accession NM_002705). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPL. Transcription Factor 19 (SC1) (TCF19, Accession XM_175251) is another VGAM1200 host target gene.

TCF19 BINDING SITE1 and TCF19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF19 BINDING SITE1 and TCF19 BINDING SITE2, designated SEQ ID:46711 and SEQ ID:46662 respectively, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3911.

[43040] Another function of VGAM1200 is therefore inhibition of Transcription Factor 19 (SC1) (TCF19, Accession XM_175251), a gene which plays an important role in the transcription of genes required for the later stages of cell cycle progression. Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF19. The function of TCF19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM299. Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM_018312) is another VGAM1200 host target gene. C11orf23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf23 BINDING SITE, designated SEQ ID:20299, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43041] Another function of VGAM1200 is therefore inhibition of

Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM_018312). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf23. DC-TM4F2 (Accession NM_030927) is another VGAM1200 host target gene. DC-TM4F2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DC-TM4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DC-TM4F2 BINDING SITE, designated SEQ ID:25198, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43042] Another function of VGAM1200 is therefore inhibition of DC-TM4F2 (Accession NM_030927). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DC-TM4F2. Di-Ras2 (Accession NM_017594) is another VGAM1200 host target gene. Di-Ras2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Di-Ras2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Di-Ras2 BINDING SITE, designated SEQ ID:19044, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43043] Another function of VGAM1200 is therefore inhibition of Di-Ras2 (Accession NM_017594). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Di-Ras2. Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063) is another VGAM1200 host target gene. EML4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EML4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EML4 BINDING SITE, designated SEQ ID:21145, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43044] Another function of VGAM1200 is therefore inhibition of Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063). Accordingly, utilities of

VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EML4. FLJ12542 (Accession NM_024899) is another VGAM1200 host target gene. FLJ12542 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12542, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12542 BINDING SITE, designated SEQ ID:24382, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43045] Another function of VGAM1200 is therefore inhibition of FLJ12542 (Accession NM_024899). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12542. FLJ12800 (Accession NM_022903) is another VGAM1200 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800

BINDING SITE, designated SEQ ID:23193, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43046] Another function of VGAM1200 is therefore inhibition of FLJ12800 (Accession NM_022903). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ13693 (Accession NM_024807) is another VGAM1200 host target gene. FLJ13693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13693 BINDING SITE, designated SEQ ID:24186, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43047] Another function of VGAM1200 is therefore inhibition of FLJ13693 (Accession NM_024807). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13693. FLJ20730 (Accession NM_017945) is another VGAM1200 host target gene. FLJ20730 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20730 BINDING SITE, designated SEQ ID:19641, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43048] Another function of VGAM1200 is therefore inhibition of FLJ20730 (Accession NM_017945). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20730. FLJ22127 (Accession NM_022775) is another VGAM1200 host target gene. FLJ22127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22127 BINDING SITE, designated SEQ ID:23040, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43049] Another function of VGAM1200 is therefore inhibition of

FLJ22127 (Accession NM_022775). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22127. FLJ23191 (Accession NM_024574) is another VGAM1200 host target gene. FLJ23191 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23191 BINDING SITE, designated SEQ ID:23801, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43050] Another function of VGAM1200 is therefore inhibition of FLJ23191 (Accession NM_024574). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23191. GMPPB (Accession XM_171044) is another VGAM1200 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45818, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43051] Another function of VGAM1200 is therefore inhibition of GMPPB (Accession XM_171044). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. KIAA1854 (Accession XM_049884) is another VGAM1200 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35536, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43052] Another function of VGAM1200 is therefore inhibition of KIAA1854 (Accession XM_049884). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. KIAA1912 (Accession XM_055636) is another

VGAM1200 host target gene. KIAA1912 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1912 BINDING SITE, designated SEQ ID:36311, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43053] Another function of VGAM1200 is therefore inhibition of KIAA1912 (Accession XM_055636). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1912. Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117) is another VGAM1200 host target gene. KLHL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL4 BINDING SITE, designated SEQ ID:21198, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ

ID:3911.

[43054] Another function of VGAM1200 is therefore inhibition of Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL4. MR (Accession NM_031212) is another VGAM1200 host target gene. MR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MR BINDING SITE, designated SEQ ID:25254, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43055] Another function of VGAM1200 is therefore inhibition of MR (Accession NM_031212). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MR. LOC129831 (Accession XM_059376) is another VGAM1200 host target gene. LOC129831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129831, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129831 BINDING SITE, designated SEQ ID:36980, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43056] Another function of VGAM1200 is therefore inhibition of LOC129831 (Accession XM_059376). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129831. LOC130644 (Accession XM_065813) is another VGAM1200 host target gene. LOC130644 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130644 BINDING SITE, designated SEQ ID:37301, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43057] Another function of VGAM1200 is therefore inhibition of LOC130644 (Accession XM_065813). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC130644. LOC151121 (Accession XM_087102) is another VGAM1200 host target gene. LOC151121 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151121 BINDING SITE, designated SEQ ID:39051, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43058] Another function of VGAM1200 is therefore inhibition of LOC151121 (Accession XM_087102). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151121. LOC151778 (Accession XM_049352) is another VGAM1200 host target gene. LOC151778 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151778, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151778 BINDING SITE, designated SEQ ID:35397, to

the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43059] Another function of VGAM1200 is therefore inhibition of LOC151778 (Accession XM_049352). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151778. LOC153396 (Accession XM_087662) is another VGAM1200 host target gene. LOC153396 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153396, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153396 BINDING SITE, designated SEQ ID:39371, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43060] Another function of VGAM1200 is therefore inhibition of LOC153396 (Accession XM_087662). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153396. LOC155340 (Accession XM_055725) is another VGAM1200 host target gene. LOC155340 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC155340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155340 BINDING SITE, designated SEQ ID:36316, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43061] Another function of VGAM1200 is therefore inhibition of LOC155340 (Accession XM_055725). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155340. LOC157867 (Accession XM_098831) is another VGAM1200 host target gene. LOC157867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157867 BINDING SITE, designated SEQ ID:41856, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43062] Another function of VGAM1200 is therefore inhibition of LOC157867 (Accession XM_098831). Accordingly, utilities

of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157867. LOC158345 (Accession XM_034640) is another VGAM1200 host target gene. LOC158345 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158345, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158345 BINDING SITE, designated SEQ ID:32132, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43063] Another function of VGAM1200 is therefore inhibition of LOC158345 (Accession XM_034640). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158345. LOC159193 (Accession XM_089436) is another VGAM1200 host target gene. LOC159193 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC159193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC159193 BINDING SITE, designated SEQ ID:39976, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43064] Another function of VGAM1200 is therefore inhibition of LOC159193 (Accession XM_089436). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159193. LOC255620 (Accession XM_173132) is another VGAM1200 host target gene. LOC255620 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255620 BINDING SITE, designated SEQ ID:46378, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43065] Another function of VGAM1200 is therefore inhibition of LOC255620 (Accession XM_173132). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255620. LOC256598 (Accession XM_172816) is another VGAM1200 host target gene. LOC256598 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256598 BINDING SITE, designated SEQ ID:46097, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43066] Another function of VGAM1200 is therefore inhibition of LOC256598 (Accession XM_172816). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256598. LOC91759 (Accession XM_040467) is another VGAM1200 host target gene. LOC91759 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91759 BINDING SITE, designated SEQ ID:33301, to the nucleotide sequence of VGAM1200 RNA, herein designated VGAM RNA, also designated SEQ ID:3911.

[43067] Another function of VGAM1200 is therefore inhibition of

LOC91759 (Accession XM_040467). Accordingly, utilities of VGAM1200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91759. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1201 (VGAM1201) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43068] VGAM1201 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1201 was detected is described hereinabove with reference to Figs. 1-8.

[43069] VGAM1201 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Nephritis Virus. VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43070] VGAM1201 gene encodes a VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1201 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1201 precursor RNA is designated SEQ ID:1187, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1187 is located at position 5950 relative to the genome of Avian Nephritis Virus.

- [43071] VGAM1201 precursor RNA folds onto itself, forming VGAM1201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43072] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1201 folded precursor RNA into VGAM1201 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide se-

quence of VGAM1201 RNA is designated SEQ ID:3912, and is provided hereinbelow with reference to the sequence listing part.

[43073] VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1201 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43074] VGAM1201 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1201 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1201 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[43075] The complementary binding of VGAM1201 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1201 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1201 host target RNA into VGAM1201 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43076] It is appreciated that VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1201 host target genes. The mRNA of each one of this plurality of VGAM1201 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1201 RNA, herein designated VGAM RNA, and which when bound by VGAM1201 RNA causes inhibition of translation of respective one or more VGAM1201 host target proteins.

[43077] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1201 gene, herein designated VGAM GENE, on one or more VGAM1201 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43078] It is yet further appreciated that a function of VGAM1201

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of viral infection by Avian Nephritis Virus. Specific functions, and accordingly utilities, of VGAM1201 correlate with, and may be deduced from, the identity of the host target genes which VGAM1201 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43079] Nucleotide sequences of the VGAM1201 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1201 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1201 are further described hereinbelow with reference to Table 1.

[43080] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1201 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1201 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43081] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1201 gene, herein designated VGAM is inhibition of expression of VGAM1201 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1201 correlate with, and may be deduced from, the identity of the target genes which VGAM1201 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43082] Exostoses (multiple)-like 2 (EXTL2, Accession NM_001439) is a VGAM1201 host target gene. EXTL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EXTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL2 BINDING SITE, designated SEQ ID:7164, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43083] A function of VGAM1201 is therefore inhibition of Exostoses (multiple)-like 2 (EXTL2, Accession NM_001439), a gene which is homologous to the EXT and EXTL genes. Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with EXTL2. The function of EXTL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM743.KIAA1580 (Accession XM_045271) is another VGAM1201 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34409, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43084] Another function of VGAM1201 is therefore inhibition of KIAA1580 (Accession XM_045271). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1879 (Accession XM_056635) is another VGAM1201 host target gene. KIAA1879 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1879, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1879 BINDING SITE, designated SEQ ID:36410, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43085] Another function of VGAM1201 is therefore inhibition of KIAA1879 (Accession XM_056635). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1879. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263) is another VGAM1201 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10455, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43086] Another function of VGAM1201 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmem-

brane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. LOC127534 (Accession XM_060532) is another VGAM1201 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37163, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43087] Another function of VGAM1201 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC151178 (Accession XM_087117) is another VGAM1201 host target gene. LOC151178 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151178, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151178 BINDING SITE, designated SEQ ID:39067, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43088] Another function of VGAM1201 is therefore inhibition of LOC151178 (Accession XM_087117). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151178. LOC158987 (Accession XM_099015) is another VGAM1201 host target gene. LOC158987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158987 BINDING SITE, designated SEQ ID:42045, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43089] Another function of VGAM1201 is therefore inhibition of LOC158987 (Accession XM_099015). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC158987. LOC221833 (Accession XM_166519) is another VGAM1201 host target gene. LOC221833 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221833 BINDING SITE, designated SEQ ID:44454, to the nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43090] Another function of VGAM1201 is therefore inhibition of LOC221833 (Accession XM_166519). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221833. LOC91661 (Accession NM_138372) is another VGAM1201 host target gene. LOC91661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91661 BINDING SITE, designated SEQ ID:28750, to the

nucleotide sequence of VGAM1201 RNA, herein designated VGAM RNA, also designated SEQ ID:3912.

[43091] Another function of VGAM1201 is therefore inhibition of LOC91661 (Accession NM_138372). Accordingly, utilities of VGAM1201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91661. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1202 (VGAM1202) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43092] VGAM1202 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1202 was detected is described hereinabove with reference to Figs. 1–8.

[43093] VGAM1202 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Nephritis Virus. VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43094] VGAM1202 gene encodes a VGAM1202 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1202 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1202 precursor RNA is designated SEQ ID:1188, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1188 is located at position 3947 relative to the genome of Avian Nephritis Virus.

- [43095] VGAM1202 precursor RNA folds onto itself, forming VGAM1202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1202 folded precursor RNA into VGAM1202 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1202 RNA is designated SEQ ID:3913, and is provided hereinbelow with reference to the sequence listing part.

[43097] VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1202 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43098] VGAM1202 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1202 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1202 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43099] The complementary binding of VGAM1202 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1202 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1202 host target RNA into VGAM1202 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43100] It is appreciated that VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1202 host target genes. The mRNA of each one of this plurality of VGAM1202 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1202 RNA, herein designated VGAM RNA, and which when bound by VGAM1202 RNA causes inhibition of translation of respective one or more VGAM1202 host target proteins.

[43101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1202 gene, herein designated VGAM GENE, on one or more VGAM1202 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[43102] It is yet further appreciated that a function of VGAM1202 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1202 include diagnosis, prevention and treatment of viral infection by Avian Nephritis Virus. Specific functions, and accordingly utilities, of VGAM1202 correlate with, and may be deduced from, the identity of the host target genes which VGAM1202 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43103] Nucleotide sequences of the VGAM1202 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1202 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1202 are further described hereinbelow with reference to Table 1.

[43104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1202 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1202 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1202 gene, herein designated VGAM is inhibition of expression of VGAM1202 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1202 correlate with, and may be deduced from, the identity of the target genes which VGAM1202 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43106] Phosphoribosyl Pyrophosphate Synthetase 1 (PRPS1, Accession NM_002764) is a VGAM1202 host target gene. PRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPS1 BINDING SITE, designated SEQ ID:8653, to the nucleotide sequence of VGAM1202 RNA, herein designated VGAM RNA, also designated SEQ ID:3913.

[43107] A function of VGAM1202 is therefore inhibition of Phosphoribosyl Pyrophosphate Synthetase 1 (PRPS1, Accession

NM_002764). Accordingly, utilities of VGAM1202 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPS1. KIAA0237 (Accession NM_014747) is another VGAM1202 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16450, to the nucleotide sequence of VGAM1202 RNA, herein designated VGAM RNA, also designated SEQ ID:3913.

[43108] Another function of VGAM1202 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1202 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1203 (VGAM1203) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[43109] VGAM1203 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1203 was detected is described hereinabove with reference to Figs. 1–8.

[43110] VGAM1203 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Scallion Virus X. VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43111] VGAM1203 gene encodes a VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1203 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1203 precursor RNA is designated SEQ ID:1189, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1189 is located at position 2316 relative to the genome of Scallion Virus X.

[43112] VGAM1203 precursor RNA folds onto itself, forming VGAM1203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43113] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1203 folded precursor RNA into VGAM1203 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1203 RNA is designated SEQ ID:3914, and is provided hereinbelow with reference to the sequence listing part.

[43114] VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1203 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[43115] VGAM1203 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1203 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1203 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[43116] The complementary binding of VGAM1203 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1203 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1203 host target RNA into VGAM1203 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43117] It is appreciated that VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1203 host target genes. The mRNA of each one of this plurality of VGAM1203 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1203 RNA, herein designated VGAM RNA, and which when bound by VGAM1203 RNA causes inhibition of translation of respective one or more VGAM1203 host target proteins.

[43118] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1203 gene, herein designated VGAM GENE, on one

or more VGAM1203 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43119] It is yet further appreciated that a function of VGAM1203 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of viral infection by Scallion Virus X. Specific functions, and accordingly utilities, of VGAM1203 correlate with, and may be deduced from, the identity of the host target genes which VGAM1203 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43120] Nucleotide sequences of the VGAM1203 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1203 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1203 are further described hereinbelow with reference to Table 1.

[43121] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1203 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1203 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43122] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1203 gene, herein designated VGAM is inhibition of expression of VGAM1203 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1203 correlate with, and may be deduced from, the identity of the target genes which VGAM1203 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43123] LOC149296 (Accession XM_086481) is a VGAM1203 host

target gene. LOC149296 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149296 BINDING SITE, designated SEQ ID:38694, to the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, also designated SEQ ID:3914.

[43124] A function of VGAM1203 is therefore inhibition of LOC149296 (Accession XM_086481). Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149296. LOC149721 (Accession XM_086649) is another VGAM1203 host target gene. LOC149721 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149721 BINDING SITE, designated SEQ ID:38810, to the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, also designated SEQ ID:3914.

[43125] Another function of VGAM1203 is therefore inhibition of LOC149721 (Accession XM_086649). Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149721. LOC153338 (Accession XM_098361) is another VGAM1203 host target gene. LOC153338 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153338, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153338 BINDING SITE, designated SEQ ID:41611, to the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, also designated SEQ ID:3914.

[43126] Another function of VGAM1203 is therefore inhibition of LOC153338 (Accession XM_098361). Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153338. LOC254413 (Accession XM_173141) is another VGAM1203 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46400, to the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, also designated SEQ ID:3914.

[43127] Another function of VGAM1203 is therefore inhibition of LOC254413 (Accession XM_173141). Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC254755 (Accession XM_173224) is another VGAM1203 host target gene. LOC254755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254755 BINDING SITE, designated SEQ ID:46487, to the nucleotide sequence of VGAM1203 RNA, herein designated VGAM RNA, also designated SEQ ID:3914.

[43128] Another function of VGAM1203 is therefore inhibition of LOC254755 (Accession XM_173224). Accordingly, utilities of VGAM1203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC254755. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1204 (VGAM1204) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43129] VGAM1204 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1204 was detected is described hereinabove with reference to Figs. 1–8.

[43130] VGAM1204 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Scallion Virus X. VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43131] VGAM1204 gene encodes a VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1204 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1204 precursor RNA is designated SEQ ID:1190, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1190 is located at position 3095 relative to the genome of Scallion Virus X.

- [43132] VGAM1204 precursor RNA folds onto itself, forming VGAM1204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43133] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1204 folded precursor RNA into VGAM1204 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1204 RNA is designated SEQ ID:3915, and is provided hereinbelow with reference to the sequence listing part.

[43134] VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1204 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43135] VGAM1204 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1204 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1204 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43136] The complementary binding of VGAM1204 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1204 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1204 host target RNA into VGAM1204 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43137] It is appreciated that VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1204 host target genes. The mRNA of each one of this plurality of VGAM1204 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1204 RNA, herein designated VGAM RNA, and which when bound by VGAM1204 RNA causes

inhibition of translation of respective one or more VGAM1204 host target proteins.

[43138] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1204 gene, herein designated VGAM GENE, on one or more VGAM1204 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43139] It is yet further appreciated that a function of VGAM1204 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1204 include diagnosis, prevention and

treatment of viral infection by Scallion Virus X. Specific functions, and accordingly utilities, of VGAM1204 correlate with, and may be deduced from, the identity of the host target genes which VGAM1204 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43140] Nucleotide sequences of the VGAM1204 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1204 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1204 are further described hereinbelow with reference to Table 1.

[43141] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1204 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1204 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43142] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1204 gene, herein designated VGAM is inhibition of expression of VGAM1204 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1204 correlate with, and may be deduced from, the identity of the target genes which VGAM1204 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43143] Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Accession NM_000782) is a VGAM1204 host target gene. CYP24 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP24 BINDING SITE, designated SEQ ID:6424, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43144] A function of VGAM1204 is therefore inhibition of Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Accession NM_000782), a gene which induces the differentiation of promyelocytes into monocytes/macrophages. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP24.

The function of CYP24 has been established by previous studies. 1,25-Dihydroxyvitamin D₃, the physiologically active form of vitamin D₃, exerts its functions through a receptor-mediated mechanism (OMIM Ref. No. 277440). In addition to its fundamental role in calcium metabolism, 1,25-(OH)₂D₃ acts on a variety of tissues. One of its most important functions is its differentiating activity. The best-characterized incidence of this activity is induction of differentiation of promyelocytes into monocytes/macrophages. 1,25-(OH)₂D₃ is biologically inactivated through a series of reactions beginning with 24-hydroxylation. 1,25-(OH)₂D₃ induces the 24-hydroxylase, whereas hypocalcemia, through increased parathyroid hormone, suppresses this enzyme. Chen et al. (1993) isolated the cDNA encoding the human 24-hydroxylase, sequenced it, and demonstrated that it is active when expressed in genetic expression systems. Using array comparative genomic hybridization (CGH), Albertson et al. (2000) resolved 2 regions of amplification within an approximately 2-Mb region of recurrent aberration at 20q13.2 in breast cancer (OMIM Ref. No. 114480). The putative oncogene ZNF217 (OMIM Ref. No. 602967) mapped to one peak, and CYP24, whose overexpression is

likely to lead to abrogation of growth control mediated by vitamin D, mapped to the other. Fine mapping demonstrated that ZNF217 lies proximal to CYP24. As transcription of CYP24 is closely coupled to the level and activity of the vitamin D receptor (VDR; 601769), Albertson et al. (2000) measured both CYP24 and VDR transcript levels using quantitative PCR in breast tumors. Expression of CYP24, normalized with respect to VDR, correlated with copy number of CYP24 in the tumors, further supporting an oncogenic role for CYP24.

[43145] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43146] Chen, K.-S.; Prahl, J. M.; DeLuca, H. F. : Isolation and expression of human 1,25-dihydroxyvitamin D3 24-hydroxylase cDNA. Proc. Nat. Acad. Sci. 90: 4543-4547, 1993. ; and

[43147] Albertson, D. G.; Ylstra, B.; Segraves, R.; Collins, C.; Dairkee, S. H.; Kowbel, D.; Kuo, W.- L.; Gray, J. W.; Pinkel, D. : Quantitative mapping of amplicon structure by array CGH identi.

[43148] Further studies establishing the function and utilities of CYP24 are found in John Hopkins OMIM database record

ID 126065, and in cited publications numbered 4359–4364 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199) is another VGAM1204 host target gene. EIF2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C1 BINDING SITE, designated SEQ ID:14504, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43149] Another function of VGAM1204 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199), a gene which plays an important role in the eukaryotic peptide chain initiation process. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2C1. The function of EIF2C1 and its association with various diseases and clinical conditions, has been established by previous studies, as described here–

inabove with reference to VGAM118. Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Accession NM_001991) is another VGAM1204 host target gene. EZH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EZH1 BINDING SITE, designated SEQ ID:7717, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43150] Another function of VGAM1204 is therefore inhibition of Enhancer of Zeste Homolog 1 (Drosophila) (EZH1, Accession NM_001991), a gene which may act in transcriptional regulation and heterochromatin maintenance. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZH1. The function of EZH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM251. Glutaredoxin (thioltransferase) (GLRX, Accession NM_002064) is another VGAM1204 host target gene. GLRX BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLRX BINDING SITE, designated SEQ ID:7831, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43151] Another function of VGAM1204 is therefore inhibition of Glutaredoxin (thioltransferase) (GLRX, Accession NM_002064), a gene which has a glutathione-disulfide oxidoreductase activity and reduces low molecular weight disulfides and proteins. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLRX. The function of GLRX has been established by previous studies. Glutaredoxin is a glutathione (GSH)-dependent hydrogen donor for ribonucleotide reductase and also catalyzes glutathione-disulfide oxidoreduction reactions in the presence of NADPH and glutathione reductase. Padilla et al. (1995) purified a human placental glutaredoxin to homogeneity and showed that its amino acid sequence was similar to that of other known mammalian

glutaredoxins (about 80% identity), with some important differences. A cDNA that encodes the entire GRX open reading frame (ORF) and flanking sequences was isolated from a human spleen cDNA library. Glutaredoxin is a small protein of 12 kD. Raghavachari et al. (2001) investigated how the expression of thioltransferase (TTase), a critical thiol repair and dethiolating enzyme, is regulated in human lens epithelial cells under oxidative stress. They also examined whether depleting the primary cellular antioxidant glutathione in these cells has any influence on TTase expression under the same conditions. They found a transient increase in TTase mRNA after 5 minutes of H_2O_2 treatment. Upregulation reached a maximum of 80% above normal by 10 minutes and gradually decreased as the cells detoxified the oxidant. They found that manipulation of cellular GSH resulted in minimal changes in TTase expression. When cells depleted of GSH were subjected to oxidative stress, TTase expression was also strongly upregulated. Raghavachari et al. (2001) concluded that the upregulation of TTase expression in lens epithelial cells could be an adaptive response of the cells to combat oxidative stress and restore the vital functions of lens proteins and enzymes. They found that such regu-

lation was independent of cellular GSH concentration.

[43152] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43153] Padilla, C. A.; Martinez-Galisteo, E.; Barcena, J. A.; Spyrou, G.; Holmgren, A. : Purification from placenta, amino acid sequence, structure comparisons and cDNA cloning of human glutaredoxin. *Europ. J. Biochem.* 227: 27–34, 1995. ; and

[43154] Raghavachari, N.; Krysan, K.; Xing K.; Lou, M. F. : Regulation of thioltransferase expression in human lens epithelial cells. *Invest. Ophthal. Vis. Sci.* 42: 1002–1008, 2001.

[43155] Further studies establishing the function and utilities of GLRX are found in John Hopkins OMIM database record ID 600443, and in cited publications numbered 10219–10221 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lectin, Galactoside-binding, Soluble, 3 Binding Protein (LGALS3BP, Accession XM_045104) is another VGAM1204 host target gene. LGALS3BP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LGALS3BP, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGALS3BP BINDING SITE, designated SEQ ID:34357, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43156] Another function of VGAM1204 is therefore inhibition of Lectin, Galactoside-binding, Soluble, 3 Binding Protein (LGALS3BP, Accession XM_045104). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGALS3BP. Nuclear Receptor Subfamily 4, Group A, Member 1 (NR4A1, Accession NM_002135) is another VGAM1204 host target gene. NR4A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR4A1 BINDING SITE, designated SEQ ID:7912, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43157] Another function of VGAM1204 is therefore inhibition of Nuclear Receptor Subfamily 4, Group A, Member 1

(NR4A1, Accession NM_002135), a gene which is a member of steroid receptor family and binds DNA. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR4A1. The function of NR4A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM897. Proprotein Convertase Subtilisin/kexin Type 2 (PCSK2, Accession NM_002594) is another VGAM1204 host target gene. PCSK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCSK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCSK2 BINDING SITE, designated SEQ ID:8459, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43158] Another function of VGAM1204 is therefore inhibition of Proprotein Convertase Subtilisin/kexin Type 2 (PCSK2, Accession NM_002594), a gene which is involved in the processing of hormone and other protein precursors at sites comprised of pairs of basic amino acid residues. Accord-

ingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCSK2. The function of PCSK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1120. Regulatory Factor X, 1 (influences HLA class II expression) (RFX1, Accession NM_002918) is another VGAM1204 host target gene. RFX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX1 BINDING SITE, designated SEQ ID:8822, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43159] Another function of VGAM1204 is therefore inhibition of Regulatory Factor X, 1 (influences HLA class II expression) (RFX1, Accession NM_002918), a gene which regulates mhc class ii gene expression and also binds to an inverted repeat (enh1) required for hepatitis b virus genes expression. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with RFX1. The function of RFX1 has been established by previous studies. The RFX1 gene product is a transactivator of the human hepatitis B viral enhancer I. Reith et al. (1994) commented that the RFX family members, particularly RFX1 and RFX3 (OMIM Ref. No. 601337), constitute the nuclear complexes referred to previously as enhancer factor C (EF-C), EP, and methylation-dependent DNA-binding protein (MDBP), or rpL30-alpha. Reith et al. (1994) identified and cloned 3 members of this gene family from both human and mouse using lambda gt11 cDNA libraries. Homology between the 3 RFX proteins is restricted largely to 5 conserved regions, including the 2 domains required for DNA binding and dimerization. Reith et al. (1994) found that RFX1, RFX2 (OMIM Ref. No. 142765), and RFX3 have similar DNA-binding specificities. The RFX monomers can heterodimerize both in vivo and in vitro, but all 3 are capable of binding DNA as monomers. They showed that the RFX1 transcript is expressed in many mouse tissues. Emery et al. (1996) reviewed RFX1, RFX5, and other members of the RFX family of DNA binding proteins.

[43160] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [43161] Reith, W.; Ucla, C.; Barras, E.; Gaud, A.; Durand, B.; Her-
rero-Sanchez, C.; Kobr, M.; Mach, B. : RFX1, a transactiva-
tor of hepatitis B virus enhancer I, belongs to a novel fam-
ily of homodimeric and heterodimeric DNA-binding pro-
teins. *Molec. Cell. Biol.* 14: 1230-1244, 1994. ; and
- [43162] Emery, P.; Durand, B.; Mach, B.; Reith, W. : RFX proteins, a
novel family of DNA binding proteins conserved in the eu-
karyotic kingdom. *Nucleic Acids Res.* 24: 803-807, 1996.
- [43163] Further studies establishing the function and utilities of
RFX1 are found in John Hopkins OMIM database record ID
600006, and in cited publications numbered 4745, 8320,
977 and 8318 listed in the bibliography section hereinbe-
low, which are also hereby incorporated by refer-
ence. Sarcosine Dehydrogenase (SARDH, Accession
NM_007101) is another VGAM1204 host target gene.
SARDH BINDING SITE is HOST TARGET binding site found
in the 5' untranslated region of mRNA encoded by
SARDH, corresponding to a HOST TARGET binding site
such as BINDING SITE I, BINDING SITE II or BINDING SITE III.
Table 2 illustrates the complementarity of the nucleotide
sequences of SARDH BINDING SITE, designated SEQ
ID:13961, to the nucleotide sequence of VGAM1204 RNA,

herein designated VGAM RNA, also designated SEQ ID:3915.

[43164] Another function of VGAM1204 is therefore inhibition of Sarcosine Dehydrogenase (SARDH, Accession NM_007101), a gene which oxidatively degrades choline to glycine. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARDH. The function of SARDH has been established by previous studies. Sarcosine dehydrogenase (SARDH; EC 1.5.99.1) is a liver mitochondrial matrix flavoenzyme that catalyzes the oxidative demethylation of sarcosine. SARDH is defective in patients with sarcosinemia (OMIM Ref. No. 268900). By homology searching, Eschenbrenner and Jorns (1999) identified a partial human infant brain SARDH cDNA. Using this partial cDNA, they isolated a full-length human liver cDNA. The predicted 918-amino acid SARDH protein contains a putative 22-amino acid mitochondrial targeting sequence, an ADP-binding site, and a stretch of 12 amino acids that matches the covalent flavin-containing peptide from rat liver Sardh. Human SARDH shares 89% amino acid sequence identity with rat liver Sardh and 34% identity with rat liver dimethylglycine dehydrogenase. Northern blot

analysis of various human adult and fetal tissues detected a 4-kb SARDH transcript at high levels in adult and fetal liver and at lower levels in adult pancreas and kidney and fetal kidney. The SARDH gene spans at least 75.3 kb and contains 21 exons. The authors identified cDNAs corresponding to alternatively spliced and polyadenylated SARDH transcripts. Eschenbrenner and Jorns (1999) identified 3 genomic sequences from 9q34 that contain the SARDH gene. The localization of the human SARDH gene to 9q34 is consistent with genetic studies using a mouse model for sarcosinemia that mapped the mouse *Sardh* gene to a region of chromosome 2 that shows homology of synteny with human 9q33–q34 (Harding et al., 1992; Brunialti et al., 1996).

[43165] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43166] Brunialti, A. L. B.; Harding, C. O.; Wolff, J. A.; Guenet, J.–L. : The mouse mutation sarcosinemia (*sar*) maps to chromosome 2 in a region homologous to human 9q33–q34. *Genomics* 36: 182–184, 1996. ; and

[43167] Eschenbrenner, M.; Jorns, M. S. : Cloning and mapping of the cDNA for human sarcosine dehydrogenase, a flavoen–

zyme defective in patients with sarcosinemia. Genomics 59: 300–308, 1999.

[43168] Further studies establishing the function and utilities of SARDH are found in John Hopkins OMIM database record ID 604455, and in cited publications numbered 9177–4765 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TOX (Accession NM_014729) is another VGAM1204 host target gene. TOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOX BINDING SITE, designated SEQ ID:16327, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43169] Another function of VGAM1204 is therefore inhibition of TOX (Accession NM_014729). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOX. Zinc Finger Protein 278 (ZNF278, Accession NM_032050) is another VGAM1204 host target gene. ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by ZNF278, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3, designated SEQ ID:25776, SEQ ID:25786 and SEQ ID:15627 respectively, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43170] Another function of VGAM1204 is therefore inhibition of Zinc Finger Protein 278 (ZNF278, Accession NM_032050), a gene which represses basal transcription as well as RNF4-mediated activation. Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF278. The function of ZNF278 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM414. Chromosome 11 Open Reading Frame 21 (C11orf21, Accession NM_014144) is another VGAM1204 host target gene. C11orf21 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C11orf21, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf21 BINDING SITE, designated SEQ ID:15427, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43171] Another function of VGAM1204 is therefore inhibition of Chromosome 11 Open Reading Frame 21 (C11orf21, Accession NM_014144). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf21. Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418) is another VGAM1204 host target gene. C11orf25 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C11orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf25 BINDING SITE, designated SEQ ID:25399, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43172] Another function of VGAM1204 is therefore inhibition of

Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf25. DKFZp434J0226 (Accession XM_051327) is another VGAM1204 host target gene. DKFZp434J0226 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434J0226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434J0226 BINDING SITE, designated SEQ ID:35806, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43173] Another function of VGAM1204 is therefore inhibition of DKFZp434J0226 (Accession XM_051327). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434J0226. FLJ11753 (Accession NM_024659) is another VGAM1204 host target gene. FLJ11753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11753, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11753 BINDING SITE, designated SEQ ID:23963, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43174] Another function of VGAM1204 is therefore inhibition of FLJ11753 (Accession NM_024659). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11753. GW112 (Accession NM_006418) is another VGAM1204 host target gene. GW112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GW112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GW112 BINDING SITE, designated SEQ ID:13129, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43175] Another function of VGAM1204 is therefore inhibition of GW112 (Accession NM_006418). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GW112. KIAA1644 (Accession XM_097892) is another VGAM1204 host target gene. KIAA1644 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1644 BINDING SITE, designated SEQ ID:41203, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43176] Another function of VGAM1204 is therefore inhibition of KIAA1644 (Accession XM_097892). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1644. MGC20235 (Accession NM_145041) is another VGAM1204 host target gene. MGC20235 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC20235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20235 BINDING SITE, designated SEQ ID:29671, to

the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43177] Another function of VGAM1204 is therefore inhibition of MGC20235 (Accession NM_145041). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20235. Serine Threonine Kinase 39 (STE20/SPS1 homolog, yeast) (STK39, Accession NM_013233) is another VGAM1204 host target gene. STK39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK39 BINDING SITE, designated SEQ ID:14895, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43178] Another function of VGAM1204 is therefore inhibition of Serine Threonine Kinase 39 (STE20/SPS1 homolog, yeast) (STK39, Accession NM_013233). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK39. LOC146146 (Accession XM_085343) is another

VGAM1204 host target gene. LOC146146 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146146 BINDING SITE, designated SEQ ID:38074, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43179] Another function of VGAM1204 is therefore inhibition of LOC146146 (Accession XM_085343). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146146. LOC149448 (Accession XM_097642) is another VGAM1204 host target gene. LOC149448 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149448 BINDING SITE, designated SEQ ID:40990, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43180] Another function of VGAM1204 is therefore inhibition of LOC149448 (Accession XM_097642). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149448. LOC169693 (Accession XM_108998) is another VGAM1204 host target gene. LOC169693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169693 BINDING SITE, designated SEQ ID:42207, to the nucleotide sequence of VGAM1204 RNA, herein designated VGAM RNA, also designated SEQ ID:3915.

[43181] Another function of VGAM1204 is therefore inhibition of LOC169693 (Accession XM_108998). Accordingly, utilities of VGAM1204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169693. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1205 (VGAM1205) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[43182] VGAM1205 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1205 was detected is described hereinabove with reference to Figs. 1–8.

[43183] VGAM1205 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Scallion Virus X. VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43184] VGAM1205 gene encodes a VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1205 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1205 precursor RNA is designated SEQ ID:1191, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1191 is located at position 2547 relative to the genome of Scallion Virus X.

[43185] VGAM1205 precursor RNA folds onto itself, forming VGAM1205 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43186] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1205 folded precursor RNA into VGAM1205 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1205 RNA is designated SEQ ID:3916, and is provided hereinbelow with reference to the sequence listing part.

[43187] VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1205 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43188] VGAM1205 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1205 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1205 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43189] The complementary binding of VGAM1205 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1205 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1205 host target RNA into VGAM1205 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43190] It is appreciated that VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1205 host target genes. The mRNA of each one of this plurality of VGAM1205 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1205 RNA, herein designated VGAM RNA, and which when bound by VGAM1205 RNA causes inhibition of translation of respective one or more VGAM1205 host target proteins.

[43191] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1205 gene, herein designated VGAM GENE, on one or more VGAM1205 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43192] It is yet further appreciated that a function of VGAM1205 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of viral infection by Scallion Virus X. Specific functions, and accordingly utilities, of VGAM1205 correlate with, and may be deduced from, the identity of the host target genes which VGAM1205 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[43193] Nucleotide sequences of the VGAM1205 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1205 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1205 are further described hereinbelow with reference to Table 1.

[43194] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1205 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1205 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43195] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1205 gene, herein designated VGAM is inhibition of expression of VGAM1205 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1205 correlate with, and may be deduced from, the identity of the target genes which VGAM1205 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43196] Aminomethyltransferase (glycine cleavage system protein T) (AMT, Accession NM_000481) is a VGAM1205 host target gene. AMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMT BINDING SITE, designated SEQ ID:6090, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43197] A function of VGAM1205 is therefore inhibition of Aminomethyltransferase (glycine cleavage system protein T) (AMT, Accession NM_000481). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMT.

Development and Differentiation Enhancing Factor 2 (DDEF2, Accession NM_003887) is another VGAM1205 host target gene. DDEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDEF2 BINDING SITE, des-

ignated SEQ ID:9969, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43198] Another function of VGAM1205 is therefore inhibition of Development and Differentiation Enhancing Factor 2 (DDEF2, Accession NM_003887), a gene which interacts with members of the Arf and Src family. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDEF2. The function of DDEF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464. GNAS Complex Locus (GNAS, Accession NM_016592) is another VGAM1205 host target gene. GNAS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAS BINDING SITE, designated SEQ ID:18677, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43199] Another function of VGAM1205 is therefore inhibition of

GNAS Complex Locus (GNAS, Accession NM_016592), a gene which transduces signals from G protein-coupled receptors and activates adenylyl cyclase. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAS. The function of GNAS has been established by previous studies. Because obesity is frequently associated with GS deficiency and GS is part of the pathway transducing the lipolytic signal through beta-adrenergic receptors, Carel et al. (1999) tested whether epinephrine resistance was part of the spectrum of hormonal resistance in patients with GS deficiency. Carel et al. (1999) measured glycerol flux, using a nonradioactive tracer dilution approach, to analyze the lipolytic response to epinephrine in 6 patients with GS deficiency and PTH resistance and compared it in 6 age-matched normal controls and 9 massively obese children. Basal glycerol production was reduced by 50%, and lipolytic response to epinephrine was reduced by 67% in GS-deficient children, as compared with controls. The degree of impairment of lipolysis was similar in GS-deficient children who were only moderately overweight and in morbidly obese children. Animal model experiments lend further support to the function of GNAS.

Yu et al. (1998) generated mice with a null allele of the *Gnas* gene. Homozygous *Gs* deficiency was embryonically lethal. Heterozygotes with maternal ($m-/+$) and paternal ($+/p-$) inheritance of the *Gnas* null allele had distinct phenotypes, suggesting that *Gnas* is an imprinted gene.

Parathyroid hormone (PTH) resistance is present in $m-/+$ but not $+/p-$ mice. Expression of the alpha subunit in the renal cortex (the site of PTH action) was markedly reduced in $m-/+$ but not in $+/p-$ mice, demonstrating that the *Gnas* paternal allele is imprinted in this tissue. *Gnas* was also imprinted in brown and white adipose tissue. The maximal physiologic response to vasopressin (urinary concentrating ability) was normal in both $m-/+$ and $+/p-$ mice and *Gnas* was not imprinted in the renal inner medulla, the site of vasopressin action. Tissue-specific imprinting of *Gnas* was likely the mechanism for variable and tissue-specific hormone resistance in the knockout mice and a similar mechanism might explain the variable phenotype in AHO.

[43200] It is appreciated that the abovementioned animal model for GNAS is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[43201] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43202] Carel, J. C.; Le Stunff, C.; Condamine, L.; Mallet, E.; Chaus-sain, J. L.; Adnot, P.; Garabedian, M.; Bougneres, P. : Re-sistance to the lipolytic action of epinephrine: a new fea-ture of protein GS deficiency. J. Clin. Endocr. Metab. 84: 4127-4131, 1999. ; and

[43203] Yu, S.; Yu, D.; Lee, E.; Eckhaus, M.; Lee, R.; Corria, Z.; Ac-cili, D.; Westphal, H.; Weinstein, L. S. : Variable and tissue-specific hormone resistance in heterotrimeric Gs protein a.

[43204] Further studies establishing the function and utilities of GNAS are found in John Hopkins OMIM database record ID 139320, and in cited publications numbered 11941-11951, 4744, 11952-11957, 12197-12200, 11463, 1394-1393, 1395-1402, 1407-1406, 1408-1415, 1466-1469, 27, 1470-1490, 2301-10 and 28 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hairless Ho-molog (mouse) (HR, Accession NM_005144) is another VGAM1205 host target gene. HR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by HR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HR BINDING SITE, designated SEQ ID:11615, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43205] Another function of VGAM1205 is therefore inhibition of Hairless Homolog (mouse) (HR, Accession NM_005144). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HR. Piccolo (presynaptic cytomatrix protein) (PCLO, Accession XM_168530) is another VGAM1205 host target gene. PCLO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCLO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCLO BINDING SITE, designated SEQ ID:45211, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43206] Another function of VGAM1205 is therefore inhibition of

Piccolo (presynaptic cytomatrix protein) (PCLO, Accession XM_168530), a gene which involves in the cycling of synaptic vesicles. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCLO. The function of PCLO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM_002836) is another VGAM1205 host target gene. PTPRA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTPRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRA BINDING SITE, designated SEQ ID:8716, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43207] Another function of VGAM1205 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, A (PTPRA, Accession NM_002836), a gene which is the human homolog of the murine PTPase. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PTPRA. The function of PTPRA has been established by previous studies. Vital cellular functions such as cell proliferation and signal transduction are regulated in part by the balance between the activities of protein-tyrosine kinases (PTK) and protein-tyrosine phosphatases (OMIM Ref. No. PTPase). Oncogenesis can result from an imbalance. There are 2 classes of PTPase molecules: low molecular weight proteins with a single conserved phosphatase domain such as T-cell protein-tyrosine phosphatase (PTPT; 176887), and high molecular weight receptor-linked PTPases with 2 tandemly repeated conserved domains separated by 56 to 57 amino acids. Examples of the latter group include leukocyte-common antigen (PTPRC; 151460) and leukocyte antigen related tyrosine phosphatase (PTPRF; 179590). Matthews et al. (1990) cloned the human homolog of the murine PTPase termed LRP by them. Its cDNA sequence predicted a protein of 793 amino acids with an unglycosylated molecular mass of 87,500 kD Matthews et al. (1990). The protein contains a 121-residue extracellular domain, a single transmembrane segment, and 2 tandem intracytoplasmic catalytic domains. By study of rodent-human somatic cell hybrids,

Jirik et al. (1990) localized PTPA/LRP to chromosome 20p13. Other family members located on chromosome 20 include SRC (OMIM Ref. No. 190090), HCK (OMIM Ref. No. 142370), and PTP1B (OMIM Ref. No. 176885). The LRP protein is ubiquitously expressed and thus likely plays a fundamental role in the physiology of all cells. With a leukocyte common antigen (LCA) probe, Kaplan et al. (1990) sequenced cDNA encoding the alpha enzyme isolated from a human brain stem cDNA library under conditions of reduced hybridization stringency. LRP encodes an 802-amino acid polypeptide. Kaplan et al. (1990) localized the RPTPase-alpha gene to human chromosome 20pter-20q12 by analysis of its segregation pattern in rodent-human somatic cell hybrids. Rao et al. (1992) re-regionalized the assignment of PTPA to the distal portion of 20p (20pter-p12) by both radioactive and fluorescence in situ hybridization. By in situ hybridization, Jirik et al. (1992) localized the PTPA gene to 20p13. With the mapping of PAX1 167411 to mouse chromosome 2, Schnittger et al. (1992) found that the homolog of PTPA is also located on mouse chromosome 2, which confirms the exceptional homology between human chromosome 20 and the distal segment of mouse chromosome 2.

[43208] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43209] Matthews, R. J.; Cahir, E. D.; Thomas, M. L. : Identification of an additional member of the protein-tyrosine-phosphatase family: evidence for alternative splicing in the tyrosine phosphatase domain. Proc. Nat. Acad. Sci. 87: 4444-4448, 1990. ; and

[43210] Schnittger, S.; Rao, V. V. N. G.; Deutsch, U.; Gruss, P.; Balling, R.; Hansmann, I. : PAX1, a member of the paired box-containing class of developmental control genes, is mapped to human ch.

[43211] Further studies establishing the function and utilities of PTPRA are found in John Hopkins OMIM database record ID 176884, and in cited publications numbered 10891-10892, 1089 and 10893-10895 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFB3, Accession NM_003243) is another VGAM1205 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFBR3 BINDING SITE, designated SEQ ID:9247, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43212] Another function of VGAM1205 is therefore inhibition of Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFBR3, Accession NM_003243), a gene which involves in capturing and retaining TGF-beta for presentation to the signaling receptors. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR3. The function of TGFBR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM139. Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM_001243) is another VGAM1205 host target gene. TNFRSF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TNFRSF8 BINDING SITE, designated SEQ ID:6908, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43213] Another function of VGAM1205 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM_001243), a gene which regulates gene expression through activation of nf-kappab. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF8. The function of TNFRSF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM154. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919) is another VGAM1205 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE4, designated SEQ ID:17188, SEQ

ID:28469, SEQ ID:28477 and SEQ ID:28452 respectively, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43214] Another function of VGAM1205 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. CLIPR-59 (Accession NM_015526) is another VGAM1205 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59 BINDING SITE, designated SEQ ID:17789, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43215] Another function of VGAM1205 is therefore inhibition of

CLIPR-59 (Accession NM_015526). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM_030881) is another VGAM1205 host target gene. DDX17 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DDX17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX17 BINDING SITE, designated SEQ ID:25157, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43216] Another function of VGAM1205 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM_030881). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX17. FLJ20452 (Accession NM_017828) is another VGAM1205 host target gene. FLJ20452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20452, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20452 BINDING SITE, designated SEQ ID:19491, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43217] Another function of VGAM1205 is therefore inhibition of FLJ20452 (Accession NM_017828). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20452. FLJ32865 (Accession NM_144613) is another VGAM1205 host target gene. FLJ32865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32865 BINDING SITE, designated SEQ ID:29432, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43218] Another function of VGAM1205 is therefore inhibition of FLJ32865 (Accession NM_144613). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ32865. KIAA0630 (Accession XM_114729) is another VGAM1205 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43063, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43219] Another function of VGAM1205 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. KIAA1029 (Accession NM_007286) is another VGAM1205 host target gene. KIAA1029 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1029 BINDING SITE, designated SEQ ID:14146, to the

nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43220] Another function of VGAM1205 is therefore inhibition of KIAA1029 (Accession NM_007286). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1029. MGC10870 (Accession NM_032301) is another VGAM1205 host target gene. MGC10870 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC10870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10870 BINDING SITE, designated SEQ ID:26081, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43221] Another function of VGAM1205 is therefore inhibition of MGC10870 (Accession NM_032301). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10870. MGC26954 (Accession NM_145025) is another VGAM1205 host target gene. MGC26954 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by MGC26954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26954 BINDING SITE, designated SEQ ID:29637, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43222] Another function of VGAM1205 is therefore inhibition of MGC26954 (Accession NM_145025). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26954. MGC4643 (Accession NM_032715) is another VGAM1205 host target gene. MGC4643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4643 BINDING SITE, designated SEQ ID:26443, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43223] Another function of VGAM1205 is therefore inhibition of MGC4643 (Accession NM_032715). Accordingly, utilities

of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4643. Nucleoporin 160kDa (NUP160, Accession XM_113678) is another VGAM1205 host target gene. NUP160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP160 BINDING SITE, designated SEQ ID:42329, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43224] Another function of VGAM1205 is therefore inhibition of Nucleoporin 160kDa (NUP160, Accession XM_113678). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP160. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792) is another VGAM1205 host target gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPNS1 BINDING SITE, designated SEQ ID:28058, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43225] Another function of VGAM1205 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. RA-GEF-2 (Accession NM_016340) is another VGAM1205 host target gene. RA-GEF-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RA-GEF-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RA-GEF-2 BINDING SITE, designated SEQ ID:18467, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43226] Another function of VGAM1205 is therefore inhibition of RA-GEF-2 (Accession NM_016340). Accordingly, utilities

of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RA-GEF-2. URG4 (Accession NM_017920) is another VGAM1205 host target gene. URG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by URG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of URG4 BINDING SITE, designated SEQ ID:19579, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43227] Another function of VGAM1205 is therefore inhibition of URG4 (Accession NM_017920). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with URG4. LOC115110 (Accession XM_049825) is another VGAM1205 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC115110 BINDING SITE, designated SEQ ID:35505, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43228] Another function of VGAM1205 is therefore inhibition of LOC115110 (Accession XM_049825). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115110. LOC147174 (Accession XM_035807) is another VGAM1205 host target gene. LOC147174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147174 BINDING SITE, designated SEQ ID:32342, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43229] Another function of VGAM1205 is therefore inhibition of LOC147174 (Accession XM_035807). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147174. LOC157376 (Accession XM_088301) is another VGAM1205 host target gene. LOC157376 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157376 BINDING SITE, designated SEQ ID:39600, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43230] Another function of VGAM1205 is therefore inhibition of LOC157376 (Accession XM_088301). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157376. LOC164397 (Accession XM_092780) is another VGAM1205 host target gene. LOC164397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164397 BINDING SITE, designated SEQ ID:40148, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43231] Another function of VGAM1205 is therefore inhibition of

LOC164397 (Accession XM_092780). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164397. LOC202451 (Accession XM_117401) is another VGAM1205 host target gene. LOC202451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202451 BINDING SITE, designated SEQ ID:43435, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43232] Another function of VGAM1205 is therefore inhibition of LOC220002 (Accession XM_166224). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220002. LOC220002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC220002 BINDING SITE, designated SEQ ID:44049, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43233] Another function of VGAM1205 is therefore inhibition of LOC220002 (Accession XM_166224). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220002. LOC253292 (Accession XM_173082) is another VGAM1205 host target gene. LOC253292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253292 BINDING SITE, designated SEQ ID:46340, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43234] Another function of VGAM1205 is therefore inhibition of LOC253292 (Accession XM_173082). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253292. LOC255294 (Accession XM_170500) is an-

other VGAM1205 host target gene. LOC255294 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255294 BINDING SITE, designated SEQ ID:45337, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43235] Another function of VGAM1205 is therefore inhibition of LOC255294 (Accession XM_170500). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255294. LOC90784 (Accession XM_034109) is another VGAM1205 host target gene. LOC90784 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90784 BINDING SITE, designated SEQ ID:32001, to the nucleotide sequence of VGAM1205 RNA, herein designated VGAM RNA, also designated SEQ ID:3916.

[43236] Another function of VGAM1205 is therefore inhibition of LOC90784 (Accession XM_034109). Accordingly, utilities of VGAM1205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90784. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1206 (VGAM1206) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43237] VGAM1206 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1206 was detected is described hereinabove with reference to Figs. 1–8.

[43238] VGAM1206 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Mosaic Virus. VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43239] VGAM1206 gene encodes a VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1206 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1206 precursor RNA is designated SEQ ID:1192, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1192 is located at position 961 relative to the genome of Clover Yellow Mosaic Virus.

[43240] VGAM1206 precursor RNA folds onto itself, forming VGAM1206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43241] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1206 folded precursor RNA into VGAM1206 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1206 RNA is designated SEQ ID:3917, and is provided hereinbelow with reference to the sequence listing part.

[43242] VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1206 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43243] VGAM1206 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1206 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1206 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43244] The complementary binding of VGAM1206 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1206 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1206 host target RNA into VGAM1206 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43245] It is appreciated that VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1206 host target genes. The mRNA of each one of this plurality of VGAM1206 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1206 RNA, herein designated VGAM RNA, and which when bound by VGAM1206 RNA causes inhibition of translation of respective one or more VGAM1206 host target proteins.

[43246] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1206 gene, herein designated VGAM GENE, on one or more VGAM1206 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43247] It is yet further appreciated that a function of VGAM1206 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1206 include diagnosis, prevention and treatment of viral infection by Clover Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1206 correlate with, and may be deduced from, the identity of the host target genes which VGAM1206 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43248] Nucleotide sequences of the VGAM1206 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1206 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1206 are further described hereinbelow with reference to Table 1.

[43249] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1206 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1206 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[43250] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1206 gene, herein designated VGAM is inhibition of expression of VGAM1206 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1206 correlate with, and may be deduced from, the identity of the target genes which VGAM1206 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43251] Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083) is a VGAM1206 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22056, to the nucleotide sequence of VGAM1206 RNA, herein designated VGAM RNA, also designated SEQ ID:3917.

[43252] A function of VGAM1206 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083). Accordingly, utilities of VGAM1206 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with XK. Programmed Cell Death 7 (PDCD7, Accession XM_050977) is another VGAM1206 host target gene. PDCD7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDCD7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDCD7 BINDING SITE, designated SEQ ID:35695, to the nucleotide sequence of VGAM1206 RNA, herein designated VGAM RNA, also designated SEQ ID:3917.

[43253] Another function of VGAM1206 is therefore inhibition of Programmed Cell Death 7 (PDCD7, Accession XM_050977). Accordingly, utilities of VGAM1206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDCD7. LOC255104 (Accession XM_170911) is another VGAM1206 host target gene. LOC255104 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255104 BINDING SITE, design-

nated SEQ ID:45686, to the nucleotide sequence of VGAM1206 RNA, herein designated VGAM RNA, also designated SEQ ID:3917.

[43254] Another function of VGAM1206 is therefore inhibition of LOC255104 (Accession XM_170911). Accordingly, utilities of VGAM1206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255104. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1207 (VGAM1207) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43255] VGAM1207 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1207 was detected is described hereinabove with reference to Figs. 1–8.

[43256] VGAM1207 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Mosaic Virus. VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43257] VGAM1207 gene encodes a VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1207 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1207 precursor RNA is designated SEQ ID:1193, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1193 is located at position 3847 relative to the genome of Clover Yellow Mosaic Virus.

[43258] VGAM1207 precursor RNA folds onto itself, forming VGAM1207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43259] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1207 folded precursor RNA into VGAM1207 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1207 RNA is designated SEQ ID:3918, and is provided hereinbelow with reference to the sequence listing part.

[43260] VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1207 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43261] VGAM1207 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1207 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1207 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43262] The complementary binding of VGAM1207 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1207 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1207 host target RNA into VGAM1207 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43263] It is appreciated that VGAM1207 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1207 host target genes. The mRNA of each one of this plurality of VGAM1207 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1207 RNA, herein designated VGAM RNA, and which when bound by VGAM1207 RNA causes inhibition of translation of respective one or more VGAM1207 host target proteins.

[43264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1207 gene, herein designated VGAM GENE, on one or more VGAM1207 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[43265] It is yet further appreciated that a function of VGAM1207 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of viral infection by Clover Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1207 correlate with, and may be deduced from, the identity of the host target genes which VGAM1207 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43266] Nucleotide sequences of the VGAM1207 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1207 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1207 are further described hereinbelow with reference to Table 1.

[43267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1207 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1207 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43268] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1207 gene, herein designated VGAM is inhibition of expression of VGAM1207 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1207 correlate with, and may be deduced from, the identity of the target genes which VGAM1207 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43269] V-ski Sarcoma Viral Oncogene Homolog (avian) (SKI, Accession NM_003036) is a VGAM1207 host target gene. SKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKI BINDING SITE, designated SEQ ID:8986, to the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43270] A function of VGAM1207 is therefore inhibition of V-ski

Sarcoma Viral Oncogene Homolog (avian) (SKI, Accession NM_003036). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKI. DKFZP434O047 (Accession NM_015594) is another VGAM1207 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434O047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17863, to the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43271] Another function of VGAM1207 is therefore inhibition of DKFZP434O047 (Accession NM_015594). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. DKFZP761E2110 (Accession NM_030953) is another VGAM1207 host target gene. DKFZP761E2110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761E2110, corresponding to a HOST TARGET bind-

ing site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761E2110 BINDING SITE, designated SEQ ID:25222, to the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43272] Another function of VGAM1207 is therefore inhibition of DKFZP761E2110 (Accession NM_030953). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761E2110. PRO2266 (Accession NM_018519) is another VGAM1207 host target gene. PRO2266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2266 BINDING SITE, designated SEQ ID:20596, to the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43273] Another function of VGAM1207 is therefore inhibition of PRO2266 (Accession NM_018519). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRO2266. ZAK (Accession NM_133646) is another VGAM1207 host target gene. ZAK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZAK BINDING SITE, designated SEQ ID:28608, to the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43274] Another function of VGAM1207 is therefore inhibition of ZAK (Accession NM_133646). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZAK. LOC147463 (Accession XM_085799) is another VGAM1207 host target gene. LOC147463 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147463 BINDING SITE, designated SEQ ID:38341, to

the nucleotide sequence of VGAM1207 RNA, herein designated VGAM RNA, also designated SEQ ID:3918.

[43275] Another function of VGAM1207 is therefore inhibition of LOC147463 (Accession XM_085799). Accordingly, utilities of VGAM1207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147463. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1208 (VGAM1208) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43276] VGAM1208 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1208 was detected is described hereinabove with reference to Figs. 1–8.

[43277] VGAM1208 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Mosaic Virus. VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43278] VGAM1208 gene encodes a VGAM1208 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1208 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1208 precursor RNA is designated SEQ ID:1194, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1194 is located at position 2694 relative to the genome of Clover Yellow Mosaic Virus.

[43279] VGAM1208 precursor RNA folds onto itself, forming VGAM1208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43280] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1208 folded precursor RNA into VGAM1208 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1208 RNA is designated SEQ ID:3919, and is provided hereinbelow with reference to the sequence listing part.

[43281] VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1208 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43282] VGAM1208 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1208 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1208 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43283] The complementary binding of VGAM1208 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1208 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1208 host target RNA into VGAM1208 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43284] It is appreciated that VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1208 host target genes. The mRNA of each one of this plurality of VGAM1208 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1208 RNA, herein designated VGAM RNA, and which when bound by VGAM1208 RNA causes inhibition of translation of respective one or more VGAM1208 host target proteins.

[43285] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1208 gene, herein designated VGAM GENE, on one or more VGAM1208 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[43286] It is yet further appreciated that a function of VGAM1208 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of viral infection by Clover Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1208 correlate with, and may be deduced from, the identity of the host target genes which VGAM1208 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43287] Nucleotide sequences of the VGAM1208 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1208 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1208 are further described hereinbelow with reference to Table 1.

[43288] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1208 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1208 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43289] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1208 gene, herein designated VGAM is inhibition of expression of VGAM1208 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1208 correlate with, and may be deduced from, the identity of the target genes which VGAM1208 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43290] BN51 (BHK21) Temperature Sensitivity Complementing (BN51T, Accession XM_113557) is a VGAM1208 host target gene. BN51T BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BN51T, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BN51T BINDING SITE, designated SEQ ID:42282, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43291] A function of VGAM1208 is therefore inhibition of BN51

(BHK21) Temperature Sensitivity Complementing (BN51T, Accession XM_113557), a gene which complements a temperature-sensitive cell cycle mutation in BHK cells. Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BN51T. The function of BN51T and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM592. Cytoplasmic Linker Associated Protein 1 (CLASP1, Accession XM_037105) is another VGAM1208 host target gene. CLASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLASP1 BINDING SITE, designated SEQ ID:32538, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43292] Another function of VGAM1208 is therefore inhibition of Cytoplasmic Linker Associated Protein 1 (CLASP1, Accession XM_037105), a gene which plays a role in the local regulation of microtubule dynamics . Accordingly, utilities

of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLASP1. The function of CLASP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM298. Integrin, Alpha 6 (ITGA6, Accession NM_000210) is another VGAM1208 host target gene. ITGA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA6 BINDING SITE, designated SEQ ID:5699, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43293] Another function of VGAM1208 is therefore inhibition of Integrin, Alpha 6 (ITGA6, Accession NM_000210). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA6. FLJ20695 (Accession NM_017929) is another VGAM1208 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20695, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19611, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43294] Another function of VGAM1208 is therefore inhibition of FLJ20695 (Accession NM_017929). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. KIAA1023 (Accession NM_017604) is another VGAM1208 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19083, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43295] Another function of VGAM1208 is therefore inhibition of KIAA1023 (Accession NM_017604). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1023. LOC114971 (Accession XM_054936) is another VGAM1208 host target gene. LOC114971 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114971 BINDING SITE, designated SEQ ID:36207, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43296] Another function of VGAM1208 is therefore inhibition of LOC114971 (Accession XM_054936). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114971. LOC155179 (Accession XM_088169) is another VGAM1208 host target gene. LOC155179 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC155179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155179 BINDING SITE, designated SEQ ID:39551, to

the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43297] Another function of VGAM1208 is therefore inhibition of LOC155179 (Accession XM_088169). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155179. LOC201516 (Accession XM_113974) is another VGAM1208 host target gene. LOC201516 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201516 BINDING SITE, designated SEQ ID:42580, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43298] Another function of VGAM1208 is therefore inhibition of LOC201516 (Accession XM_113974). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201516. LOC222865 (Accession XM_167242) is another VGAM1208 host target gene. LOC222865 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC222865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222865 BINDING SITE, designated SEQ ID:44620, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43299] Another function of VGAM1208 is therefore inhibition of LOC222865 (Accession XM_167242). Accordingly, utilities of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222865. LOC257464 (Accession XM_116972) is another VGAM1208 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43161, to the nucleotide sequence of VGAM1208 RNA, herein designated VGAM RNA, also designated SEQ ID:3919.

[43300] Another function of VGAM1208 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities

of VGAM1208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1209 (VGAM1209) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43301] VGAM1209 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1209 was detected is described hereinabove with reference to Figs. 1-8.

[43302] VGAM1209 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Mosaic Virus. VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43303] VGAM1209 gene encodes a VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1209 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1209 precursor RNA is designated SEQ ID:1195, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1195 is located at position 5426 relative to the genome of Clover Yellow Mosaic Virus.

- [43304] VGAM1209 precursor RNA folds onto itself, forming VGAM1209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43305] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1209 folded precursor RNA into VGAM1209 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1209 RNA is designated SEQ ID:3920, and

is provided hereinbelow with reference to the sequence listing part.

[43306] VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1209 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[43307] VGAM1209 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1209 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1209 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43308] The complementary binding of VGAM1209 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1209 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1209 host target RNA into VGAM1209 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43309] It is appreciated that VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1209 host target genes. The mRNA of each one of this plurality of VGAM1209 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1209 RNA, herein designated VGAM RNA, and which when bound by VGAM1209 RNA causes inhibition of translation of respective one or more VGAM1209 host target proteins.

[43310] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1209 gene, herein designated VGAM GENE, on one or more VGAM1209 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43311] It is yet further appreciated that a function of VGAM1209 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of viral infection by Clover Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1209 correlate with, and may be deduced from, the identity of the host target genes which VGAM1209 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43312] Nucleotide sequences of the VGAM1209 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1209 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1209 are further described hereinbelow with reference to Table 1.

[43313] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1209 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1209 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43314] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1209 gene, herein designated VGAM is inhibition of expression of VGAM1209 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1209 correlate with, and may be deduced from, the identity of the target genes which VGAM1209 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43315] Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2A (GRIN2A, Accession NM_000833) is a VGAM1209 host target gene. GRIN2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2A BINDING SITE, designated SEQ ID:6489, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43316] A function of VGAM1209 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2A (GRIN2A, Accession NM_000833), a gene which modulates the efficiency of synaptic plasticity. Accordingly, utilities of VGAM1209 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with GRIN2A. The function of GRIN2A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481) is another VGAM1209 host target gene. TCF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE, designated SEQ ID:13201, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43317] Another function of VGAM1209 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118. Tumor Protein P53 (Li-Fraumeni syndrome) (TP53, Accession NM_000546) is another VGAM1209 host target gene. TP53 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TP53, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53 BINDING SITE, designated SEQ ID:6151, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43318] Another function of VGAM1209 is therefore inhibition of Tumor Protein P53 (Li-Fraumeni syndrome) (TP53, Accession NM_000546). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53. Tripartite Motif-containing 34 (TRIM34, Accession NM_021616) is another VGAM1209 host target gene. TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2, designated SEQ ID:22249 and SEQ ID:28173 respectively, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43319] Another function of VGAM1209 is therefore inhibition of Tripartite Motif-containing 34 (TRIM34, Accession NM_021616). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM34. KIAA1016 (Accession XM_166260) is another VGAM1209 host target gene. KIAA1016 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1016 BINDING SITE, designated SEQ ID:44085, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43320] Another function of VGAM1209 is therefore inhibition of KIAA1016 (Accession XM_166260). Accordingly, utilities

of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1016. LEC3 (Accession NM_015236) is another VGAM1209 host target gene. LEC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEC3 BINDING SITE, designated SEQ ID:17566, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43321] Another function of VGAM1209 is therefore inhibition of LEC3 (Accession NM_015236). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEC3. MGC22014 (Accession XM_035307) is another VGAM1209 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING

SITE, designated SEQ ID:32217, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43322] Another function of VGAM1209 is therefore inhibition of MGC22014 (Accession XM_035307). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22014. Protein-O-mannosyltransferase 1 (POMT1, Accession NM_007171) is another VGAM1209 host target gene. POMT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMT1 BINDING SITE, designated SEQ ID:14016, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43323] Another function of VGAM1209 is therefore inhibition of Protein-O-mannosyltransferase 1 (POMT1, Accession NM_007171). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMT1. LOC143173

(Accession XM_016685) is another VGAM1209 host target gene. LOC143173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143173 BINDING SITE, designated SEQ ID:30269, to the nucleotide sequence of VGAM1209 RNA, herein designated VGAM RNA, also designated SEQ ID:3920.

[43324] Another function of VGAM1209 is therefore inhibition of LOC143173 (Accession XM_016685). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143173. LOC202451 (Accession XM_117401) is another VGAM1209 host target gene. LOC202451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202451 BINDING SITE, designated SEQ ID:43437, to the nucleotide sequence of VGAM1209 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3920.

[43325] Another function of VGAM1209 is therefore inhibition of LOC202451 (Accession XM_117401). Accordingly, utilities of VGAM1209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202451. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1210 (VGAM1210) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43326] VGAM1210 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1210 was detected is described hereinabove with reference to Figs. 1–8.

[43327] VGAM1210 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43328] VGAM1210 gene encodes a VGAM1210 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1210 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1210 precursor RNA is designated SEQ ID:1196, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1196 is located at position 134784 relative to the genome of Camelpox Virus.

- [43329] VGAM1210 precursor RNA folds onto itself, forming VGAM1210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43330] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1210 folded precursor RNA into VGAM1210 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1210 RNA is designated SEQ ID:3921, and is provided hereinbelow with reference to the sequence listing part.

[43331] VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1210 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43332] VGAM1210 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1210 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1210 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43333] The complementary binding of VGAM1210 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1210 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1210 host target RNA into VGAM1210 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43334] It is appreciated that VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1210 host target genes. The mRNA of

each one of this plurality of VGAM1210 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1210 RNA, herein designated VGAM RNA, and which when bound by VGAM1210 RNA causes inhibition of translation of respective one or more VGAM1210 host target proteins.

[43335] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1210 gene, herein designated VGAM GENE, on one or more VGAM1210 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[43336] It is yet further appreciated that a function of VGAM1210 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1210 correlate with, and may be deduced from, the identity of the host target genes which VGAM1210 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43337] Nucleotide sequences of the VGAM1210 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1210 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1210 are further described hereinbelow with reference to Table 1.

[43338] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1210 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1210 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43339] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1210 gene, herein designated VGAM is inhibition of expression of VGAM1210 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1210 correlate with, and may be deduced from, the identity of the target genes which VGAM1210 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43340] BDG-29 (Accession XM_051343) is a VGAM1210 host target gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35816, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43341] A function of VGAM1210 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BDG-29. Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940) is another VGAM1210 host target gene. C21orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf6 BINDING SITE, designated SEQ ID:18855, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43342] Another function of VGAM1210 is therefore inhibition of Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf6. DKFZp434D177 (Accession NM_032264) is another VGAM1210 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:26007, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43343] Another function of VGAM1210 is therefore inhibition of DKFZp434D177 (Accession NM_032264). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434D177. HSA249128 (Accession NM_017583) is another VGAM1210 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19027, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43344] Another function of VGAM1210 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with HSA249128. KIAA1634 (Accession XM_032749) is another VGAM1210 host target gene. KIAA1634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1634 BINDING SITE, designated SEQ ID:31751, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43345] Another function of VGAM1210 is therefore inhibition of KIAA1634 (Accession XM_032749). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1634. KIAA1941 (Accession XM_059318) is another VGAM1210 host target gene. KIAA1941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1941 BINDING SITE, designated SEQ ID:36951, to the

nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43346] Another function of VGAM1210 is therefore inhibition of KIAA1941 (Accession XM_059318). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1941. PRO2533 (Accession NM_018629) is another VGAM1210 host target gene. PRO2533 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2533 BINDING SITE, designated SEQ ID:20702, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43347] Another function of VGAM1210 is therefore inhibition of PRO2533 (Accession NM_018629). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2533. LOC151201 (Accession XM_098021) is another VGAM1210 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41323, to the nucleotide sequence of VGAM1210 RNA, herein designated VGAM RNA, also designated SEQ ID:3921.

[43348] Another function of VGAM1210 is therefore inhibition of LOC151201 (Accession XM_098021). Accordingly, utilities of VGAM1210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1211 (VGAM1211) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43349] VGAM1211 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1211 was detected is described hereinabove with reference to Figs. 1-8.

[43350] VGAM1211 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Camelpox Virus.

VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43351] VGAM1211 gene encodes a VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1211 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1211 precursor RNA is designated SEQ ID:1197, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1197 is located at position 138029 relative to the genome of Camelpox Virus.

[43352] VGAM1211 precursor RNA folds onto itself, forming VGAM1211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43353] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1211 folded precursor RNA into VGAM1211 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1211 RNA is designated SEQ ID:3922, and is provided hereinbelow with reference to the sequence listing part.

[43354] VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1211 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43355] VGAM1211 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1211 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1211 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43356] The complementary binding of VGAM1211 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1211 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1211

host target RNA into VGAM1211 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43357] It is appreciated that VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1211 host target genes. The mRNA of each one of this plurality of VGAM1211 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1211 RNA, herein designated VGAM RNA, and which when bound by VGAM1211 RNA causes inhibition of translation of respective one or more VGAM1211 host target proteins.

[43358] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1211 gene, herein designated VGAM GENE, on one or more VGAM1211 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43359] It is yet further appreciated that a function of VGAM1211 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1211 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1211 correlate with, and may be deduced from, the identity of the host target genes which VGAM1211 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43360] Nucleotide sequences of the VGAM1211 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1211 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1211 are further

described hereinbelow with reference to Table 1.

[43361] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1211 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1211 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43362] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1211 gene, herein designated VGAM is inhibition of expression of VGAM1211 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1211 correlate with, and may be deduced from, the identity of the target genes which VGAM1211 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43363] NDRG Family Member 3 (NDRG3, Accession NM_022477) is a VGAM1211 host target gene. NDRG3 BINDING SITE1 and NDRG3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of NDRG3 BINDING SITE1 and NDRG3 BINDING SITE2, designated SEQ ID:22845 and SEQ ID:25720 respectively, to the nucleotide sequence of VGAM1211 RNA, herein designated VGAM RNA, also designated SEQ ID:3922.

[43364] A function of VGAM1211 is therefore inhibition of NDRG Family Member 3 (NDRG3, Accession NM_022477). Accordingly, utilities of VGAM1211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1212 (VGAM1212) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43365] VGAM1212 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1212 was detected is described hereinabove with reference to Figs. 1-8.

[43366] VGAM1212 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus. VGAM1212 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[43367] VGAM1212 gene encodes a VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1212 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1212 precursor RNA is designated SEQ ID:1198, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1198 is located at position 133579 relative to the genome of Camelpox Virus.

[43368] VGAM1212 precursor RNA folds onto itself, forming VGAM1212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43369] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1212 folded precursor RNA into VGAM1212

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1212 RNA is designated SEQ ID:3923, and is provided hereinbelow with reference to the sequence listing part.

[43370] VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1212 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43371] VGAM1212 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1212 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1212 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43372] The complementary binding of VGAM1212 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1212 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1212 host target RNA into VGAM1212 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[43373] It is appreciated that VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1212 host target genes. The mRNA of each one of this plurality of VGAM1212 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1212 RNA, herein designated VGAM RNA, and which when bound by VGAM1212 RNA causes inhibition of translation of respective one or more VGAM1212 host target proteins.

[43374] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1212 gene, herein designated VGAM GENE, on one or more VGAM1212 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43375] It is yet further appreciated that a function of VGAM1212 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1212 correlate with, and may be deduced from, the identity of the host target genes which VGAM1212 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43376] Nucleotide sequences of the VGAM1212 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1212 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1212 are further described hereinbelow with reference to Table 1.

[43377] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1212 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1212 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43378] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1212 gene, herein designated VGAM is inhibition of expression of VGAM1212 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1212 correlate with, and may be deduced from, the identity of the target genes which VGAM1212 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43379] Coagulation Factor III (thromboplastin, tissue factor) (F3, Accession XM_040465) is a VGAM1212 host target gene. F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F3 BINDING SITE, designated SEQ ID:33296, to the nucleotide sequence of VGAM1212 RNA, herein designated

VGAM RNA, also designated SEQ ID:3923.

- [43380] A function of VGAM1212 is therefore inhibition of Coagulation Factor III (thromboplastin, tissue factor) (F3, Accession XM_040465), a gene which functions in normal hemostasis. Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F3. The function of F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM817. Serine/threonine Kinase 6 (STK6, Accession NM_003600) is another VGAM1212 host target gene. STK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK6 BINDING SITE, designated SEQ ID:9654, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.
- [43381] Another function of VGAM1212 is therefore inhibition of Serine/threonine Kinase 6 (STK6, Accession NM_003600), a gene which is serine/threonine kinase 6 which is most

highly expressed during mitosis. Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK6. The function of STK6 has been established by previous studies. Kimura et al. (1997) cloned a cDNA encoding a novel human serine/threonine kinase, STK6, which has high homology with Aurora and Ipl1 kinases. Mutations in these yeast kinases are known to cause abnormal spindle formation and missegregation of chromosomes. Northern and Western blotting analyses revealed a high level of STK6 expression product in testis and proliferating culture cells such as HeLa cells. The endogenous levels of STK6 protein and protein kinase activity were tightly regulated during cell cycle progression in HeLa cells. The protein was upregulated during G2/M and rapidly reduced after mitosis. Immunofluorescence studies revealed specific localization of STK6 protein to the spindle pole region during mitosis. The results suggested that STK6, like Aurora and Ipl1, is involved in cell growth and/or chromosome segregation. By fluorescence in situ hybridization, Kimura et al. (1997) showed that this mitotic centrosomal protein kinase, also referred to as ALK, is represented by 2 signals in chromosome bands 20q13.2-q13.3 and 1q41-q42. So-

matic cell hybrid panel analyses showed that the functional gene is on chromosome 20 and a processed pseudogene (STK6P) on chromosome 1.

[43382] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43383] Kimura, M.; Kotani, S.; Hattori, T.; Sumi, N.; Yoshioka, T.; Todokoro, T.; Okano, Y. : Cell cycle-dependent expression and spindle pole localization of a novel human protein kinase Aik, related to Aurora of *Drosophila* and yeast Ipl1. *J. Biol. Chem.* 272: 13766–13771, 1997. ; and

[43384] Kimura, M.; Matsuda, Y.; Eki, T.; Yoshioka, T.; Okumura, K.; Hanaoka, F.; Okano, Y. : Assignment of STK6 to human chromosome 20q13.2–q13.3 and a pseudogene STK6P to 1q41–q42. *Cytogenet.*

[43385] Further studies establishing the function and utilities of STK6 are found in John Hopkins OMIM database record ID 602687, and in cited publications numbered 6225 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10719 (Accession XM_031328) is another VGAM1212 host target gene. FLJ10719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

FLJ10719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10719 BINDING SITE, designated SEQ ID:31339, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.

[43386] Another function of VGAM1212 is therefore inhibition of FLJ10719 (Accession XM_031328). Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10719. FLJ23323 (Accession NM_024654) is another VGAM1212 host target gene. FLJ23323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23323 BINDING SITE, designated SEQ ID:23953, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.

[43387] Another function of VGAM1212 is therefore inhibition of FLJ23323 (Accession NM_024654). Accordingly, utilities of

VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23323. LOC149721 (Accession XM_086649) is another VGAM1212 host target gene. LOC149721 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149721 BINDING SITE, designated SEQ ID:38808, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.

[43388] Another function of VGAM1212 is therefore inhibition of LOC149721 (Accession XM_086649). Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149721. LOC202459 (Accession NM_145303) is another VGAM1212 host target gene. LOC202459 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC202459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC202459 BINDING SITE, designated SEQ ID:29814, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.

[43389] Another function of VGAM1212 is therefore inhibition of LOC202459 (Accession NM_145303). Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202459. LOC254735 (Accession XM_171051) is another VGAM1212 host target gene. LOC254735 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254735 BINDING SITE, designated SEQ ID:45837, to the nucleotide sequence of VGAM1212 RNA, herein designated VGAM RNA, also designated SEQ ID:3923.

[43390] Another function of VGAM1212 is therefore inhibition of LOC254735 (Accession XM_171051). Accordingly, utilities of VGAM1212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254735. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1213 (VGAM1213) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43391] VGAM1213 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1213 was detected is described hereinabove with reference to Figs. 1–8.

[43392] VGAM1213 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Strawberry Mottle Virus. VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43393] VGAM1213 gene encodes a VGAM1213 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1213 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1213 precursor RNA is designated SEQ ID:1199, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1199 is located at position 4590 relative to the

genome of Strawberry Mottle Virus.

[43394] VGAM1213 precursor RNA folds onto itself, forming VGAM1213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43395] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1213 folded precursor RNA into VGAM1213 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1213 RNA is designated SEQ ID:3924, and is provided hereinbelow with reference to the sequence listing part.

[43396] VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1213 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43397] VGAM1213 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1213 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1213 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43398] The complementary binding of VGAM1213 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1213 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1213 host target RNA into VGAM1213 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43399] It is appreciated that VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1213 host target genes. The mRNA of each one of this plurality of VGAM1213 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1213 RNA, herein designated VGAM RNA, and which when bound by VGAM1213 RNA causes inhibition of translation of respective one or more VGAM1213 host target proteins.

[43400] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1213 gene, herein designated VGAM GENE, on one or more VGAM1213 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43401] It is yet further appreciated that a function of VGAM1213 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGAM1213

correlate with, and may be deduced from, the identity of the host target genes which VGAM1213 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43402] Nucleotide sequences of the VGAM1213 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1213 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1213 are further described hereinbelow with reference to Table 1.

[43403] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1213 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1213 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43404] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1213 gene, herein designated VGAM is inhibition of expression of VGAM1213 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1213 correlate with, and may be deduced

from, the identity of the target genes which VGAM1213 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43405] Phosphatidylinositol-4-phosphate 5-kinase, Type I, Beta (PIP5K1B, Accession NM_003558) is a VGAM1213 host target gene. PIP5K1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP5K1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K1B BINDING SITE, designated SEQ ID:9605, to the nucleotide sequence of VGAM1213 RNA, herein designated VGAM RNA, also designated SEQ ID:3924.

[43406] A function of VGAM1213 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type I, Beta (PIP5K1B, Accession NM_003558), a gene which catalyses the phosphorylation of phosphatidylinositol-4-phosphate to form phosphatidylinositol-4,5-bisphosphate. Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K1B. The function of PIP5K1B has been established by previous studies. Carvajal et al. (1995) re-

ported the isolation of a gene from the region of the genome associated with Friedreich ataxia (FRDA; 229300). Expression was found to be complex, with multiple transcripts detected in a variety of tissues and evidence of alternative splicing and developmental control. The predicted amino acid sequence for the 2.7-kb transcript showed a marked homology to the deduced amino acid sequence of the MSS4 protein of *Saccharomyces cerevisiae*, which had been proposed to function in the phosphoinositide cycle, thus suggesting a potential role for the human homolog in signal transduction. Although no evidence of mutation was detected in the transcript, the sequence (which they designated STM7.I) represented only one of the shorter alternatively spliced species identified by Northern analysis and direct sequencing. Carvajal et al. (1996) reported that the X25 (frataxin-encoding) gene described by Campuzano et al. (1996) and shown to be associated with mutations in FRDA patients comprises part of a gene that they had previously identified and named STM7. They reported that the transcription of both STM7 and X25 occurs from the centromere toward the telomere, that the reported sequences of STM7 and X25 did not represent a full-length transcript, that multiple transcripts

for each of these genes are present in Northern blots, and that several of these transcripts are of similar size. Carvajal et al. (1996) also reported that less than 10 kb separates the CpG island identified in the X25/exon 1 from the 3-prime end of STM7/exon 16. They further demonstrated that the recombinant protein corresponding to the STM7.1 transcript has phosphatidylinositol-4-phosphate 5-kinase activity. See 606829 for further discussion of the relationship between STM7 and FRDA.

[43407] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43408] Campuzano, V.; Montermini, L.; Molto, M. D.; Pianese, L.; Cossee, M.; Cavalcanti, F.; Monros, E.; Rodius, F.; Duclos, F.; Monticelli, A.; Zara, F.; Canizares, J.; Koutnikova, H.; Bidichandani, S. I.; Gellera, C.; Brice, A.; Trouillas, P.; De Michele, G.; Filla, A.; De Frutos, R.; Palau, F.; Patel, P. I.; Di Donato, S.; Mandel, J. -L.; Coccozza, S.; Koenig, M.; Pandolfo, M. : Friedreich's ataxia: autosomal recessive disease caused by an intronic GAA triplet repeat expansion. *Science* 271: 1423-1427, 1996. ; and

[43409] Carvajal, J. J.; Pook, M. A.; dos Santos, M.; Doudney, K.; Hillermann, R.; Minogue, S.; Williamson, R.; Hsuan, J. J.;

Chamberlain, S. : The Friedreich's ataxia gene encodes a novel phos.

[43410] Further studies establishing the function and utilities of PIP5K1B are found in John Hopkins OMIM database record ID 602745, and in cited publications numbered 8277–2401 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1463 (Accession XM_051160) is another VGAM1213 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35767, to the nucleotide sequence of VGAM1213 RNA, herein designated VGAM RNA, also designated SEQ ID:3924.

[43411] Another function of VGAM1213 is therefore inhibition of KIAA1463 (Accession XM_051160). Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM_032918) is another

VGAM1213 host target gene. RERG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RERG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RERG BINDING SITE, designated SEQ ID:26737, to the nucleotide sequence of VGAM1213 RNA, herein designated VGAM RNA, also designated SEQ ID:3924.

[43412] Another function of VGAM1213 is therefore inhibition of RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM_032918). Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERG. LOC221474 (Accession XM_166464) is another VGAM1213 host target gene. LOC221474 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221474 BINDING SITE, designated SEQ ID:44378, to the nucleotide sequence of VGAM1213 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3924.

[43413] Another function of VGAM1213 is therefore inhibition of LOC221474 (Accession XM_166464). Accordingly, utilities of VGAM1213 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221474. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1214 (VGAM1214) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43414] VGAM1214 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1214 was detected is described hereinabove with reference to Figs. 1–8.

[43415] VGAM1214 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43416] VGAM1214 gene encodes a VGAM1214 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1214 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1214 precursor RNA is designated SEQ ID:1200, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1200 is located at position 190571 relative to the genome of Tupaia Herpesvirus.

- [43417] VGAM1214 precursor RNA folds onto itself, forming VGAM1214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43418] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1214 folded precursor RNA into VGAM1214 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1214 RNA is designated SEQ ID:3925, and is provided hereinbelow with reference to the sequence listing part.

[43419] VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1214 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43420] VGAM1214 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1214 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1214 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43421] The complementary binding of VGAM1214 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1214 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1214 host target RNA into VGAM1214 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43422] It is appreciated that VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1214 host target genes. The mRNA of

each one of this plurality of VGAM1214 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1214 RNA, herein designated VGAM RNA, and which when bound by VGAM1214 RNA causes inhibition of translation of respective one or more VGAM1214 host target proteins.

[43423] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1214 gene, herein designated VGAM GENE, on one or more VGAM1214 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[43424] It is yet further appreciated that a function of VGAM1214 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1214 correlate with, and may be deduced from, the identity of the host target genes which VGAM1214 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43425] Nucleotide sequences of the VGAM1214 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1214 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1214 are further described hereinbelow with reference to Table 1.

[43426] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1214 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1214 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43427] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1214 gene, herein designated VGAM is inhibition of expression of VGAM1214 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1214 correlate with, and may be deduced from, the identity of the target genes which VGAM1214 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43428] Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409) is a VGAM1214 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10667, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43429] A function of VGAM1214 is therefore inhibition of Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409). Accordingly, utilities of VGAM1214 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. EphA8 (EPHA8, Accession NM_020526) is another VGAM1214 host target gene. EPHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA8 BINDING SITE, designated SEQ ID:21744, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43430] Another function of VGAM1214 is therefore inhibition of EphA8 (EPHA8, Accession NM_020526), a gene which encodes Eph-related receptor tyrosine kinase A8. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA8. The function of EPHA8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM494. Fanconi Anemia, Complementation Group A (FANCA, Accession NM_000135) is another VGAM1214 host target gene. FANCA BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCA BINDING SITE, designated SEQ ID:5630, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43431] Another function of VGAM1214 is therefore inhibition of Fanconi Anemia, Complementation Group A (FANCA, Accession NM_000135). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCA. GLI-Kruppel Family Member GLI2 (GLI2, Accession NM_030379) is another VGAM1214 host target gene. GLI2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GLI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLI2 BINDING SITE, designated SEQ ID:24936, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43432] Another function of VGAM1214 is therefore inhibition of GLI-Kruppel Family Member GLI2 (GLI2, Accession NM_030379), a gene which may promote tax-dependent transcription of T-cell leukemia virus type 1 genes. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLI2. The function of GLI2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM465. Homeo Box D1 (HOXD1, Accession NM_024501) is another VGAM1214 host target gene. HOXD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD1 BINDING SITE, designated SEQ ID:23696, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43433] Another function of VGAM1214 is therefore inhibition of Homeo Box D1 (HOXD1, Accession NM_024501), a gene which is part of a developmental regulatory system . Ac-

cordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD1. The function of HOXD1 has been established by previous studies. Both children studied by Del Campo et al. (1999) were heterozygous for a deletion that eliminated at least 8 (HOXD3–HOXD13) of the 9 genes in the HOXD cluster. Del Campo et al. (1999) suspected that the entire cluster was deleted and that the deletion included the proximally adjacent HOXD–complex gene EVX2 (OMIM Ref. No. 142991). The hypothesis that haploinsufficiency for HOXD–cluster genes was responsible in part for the malformations was supported by the expression patterns of these genes in early vertebrate embryos. However, the involvement of additional genes in the region could explain the discordance, in severity, between the 2 patients and the milder, nonpolarized phenotypes present in mice hemizygous for HoxD cluster genes. Del Campo et al. (1999) noted that mutations in HOXD13 (OMIM Ref. No. 142989) are responsible for type II syndactyly (OMIM Ref. No. 186000). Zakany et al. (2001) showed that Hoxd1 and other Hox genes in the mouse display dynamic stripes of expression within presomitic mesoderm. They stated that the underlying transcriptional

bursts may reflect the mechanism that coordinates Hox gene activation with somitogenesis. This mechanism appeared to depend upon Notch signaling, as mice deficient for Rbpjk (OMIM Ref. No. 147183), the effector of the Notch pathway, showed severely reduced Hoxd gene expression in presomitic mesoderm. These results suggested a molecular link between Hox gene activation and the segmentation clock. Such a linkage would efficiently keep in phase the production of novel segments with their morphologic specification.

[43434] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43435] Del Campo, M.; Jones, M. C.; Veraksa, A. N.; Curry, C. J.; Jones, K. L.; Mascarello, J. T.; Ali-Kahn-Catts, Z.; Drumheller, T.; McGinnis, W. : Monodactylous limbs and abnormal genitalia are associated with hemizygosity for the human 2q31 region that includes the HOXD cluster. Am. J. Hum. Genet. 65: 104–110, 1999. ; and

[43436] Zakany, J.; Kmita, M.; Alarcon, P.; de la Pompa, J.-L.; Duboule, D. : Localized and transient transcription of Hox genes suggests a link between patterning and the segmentation clock.

[43437] Further studies establishing the function and utilities of HOXD1 are found in John Hopkins OMIM database record ID 142987, and in cited publications numbered 11321–11322 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kruppel-like Factor 8 (KLF8, Accession NM_007250) is another VGAM1214 host target gene. KLF8 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KLF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLF8 BINDING SITE, designated SEQ ID:14123, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43438] Another function of VGAM1214 is therefore inhibition of Kruppel-like Factor 8 (KLF8, Accession NM_007250). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLF8. LENG4 (Accession NM_024298) is another VGAM1214 host target gene. LENG4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LENG4, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23581, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43439] Another function of VGAM1214 is therefore inhibition of LENG4 (Accession NM_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. Neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease) (NF1, Accession NM_000267) is another VGAM1214 host target gene. NF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NF1 BINDING SITE, designated SEQ ID:5812, to the nu-

cleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43440] Another function of VGAM1214 is therefore inhibition of Neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease) (NF1, Accession NM_000267). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NF1. 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187) is another VGAM1214 host target gene. OAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS3 BINDING SITE, designated SEQ ID:12859, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43441] Another function of VGAM1214 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of

VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS3. The function of OAS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM309. Phosphodiesterase 4A, CAMP-specific (phosphodiesterase E2 dunce homolog, Drosophila) (PDE4A, Accession NM_006202) is another VGAM1214 host target gene. PDE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4A BINDING SITE, designated SEQ ID:12876, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43442] Another function of VGAM1214 is therefore inhibition of Phosphodiesterase 4A, CAMP-specific (phosphodiesterase E2 dunce homolog, Drosophila) (PDE4A, Accession NM_006202), a gene which is a CAMP-specific phosphodiesterase. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with PDE4A. The function of PDE4A has been established by previous studies. See 600128. Livi et al. (1990) isolated a cDNA for a cyclic AMP phosphodiesterase from human monocytes. Obernolte et al. (1993) identified the monocyte clone as the homolog of rat Pde4a. Milatovich et al. (1994) assigned the PDE4A gene to human chromosome 19 by Southern analysis of somatic cell hybrid lines and to mouse chromosome 9 by Southern analysis of recombinant inbred (RI) mouse strains. Horton et al. (1995) confirmed the localization of PDE4A to chromosome 19 by analysis of a human/hamster somatic cell hybrid panel and using fluorescence in situ hybridization, regionalized the gene to 19p13.2-q12. The full-length clone for PDE4A was reported by Bolger et al. (1993). The difference in sequence within the 5-prime region of the open reading frame reported by Bolger et al. (1993) and Livi et al. (1990) was examined by Sullivan et al. (1994), who confirmed the Bolger sequence. Wilson et al. (1994) characterized the enzyme.

[43443] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43444] Milatovich, A.; Bolger, G.; Michaeli, T.; Francke, U. : Chro-

mosome localizations of genes for five cAMP-specific phosphodiesterases in man and mouse. Somat. Cell Molec. Genet. 20: 75–86, 1994. ; and

[43445] Bolger, G.; Michaeli, T.; Martins, T.; St. John, T.; Steiner, B.; Rodgers, L.; Riggs, M.; Wigler, M.; Ferguson, K. : A family of human phosphodiesterases homologous to the dunce learning.

[43446] Further studies establishing the function and utilities of PDE4A are found in John Hopkins OMIM database record ID 600126, and in cited publications numbered 4888–134 and 12445–1344 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727) is another VGAM1214 host target gene. SLC24A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC24A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC24A1 BINDING SITE, designated SEQ ID:11102, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43447] Another function of VGAM1214 is therefore inhibition of Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727), a gene which is a critical component of the visual transduction cascade, controlling the calcium concentration of outer segments during light and darkness. Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC24A1. The function of SLC24A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM142. Angiotensin II Receptor-like 2 (AGTRL2, Accession NM_005162) is another VGAM1214 host target gene. AGTRL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AGTRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGTRL2 BINDING SITE, designated SEQ ID:11645, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43448] Another function of VGAM1214 is therefore inhibition of

Angiotensin II Receptor-like 2 (AGTRL2, Accession NM_005162). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTRL2. Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837) is another VGAM1214 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16854, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43449] Another function of VGAM1214 is therefore inhibition of Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. Chromosome 21 Open Reading Frame 93 (C21orf93, Accession NM_145179) is another VGAM1214 host target gene. C21orf93 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C21orf93, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf93 BINDING SITE, designated SEQ ID:29740, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43450] Another function of VGAM1214 is therefore inhibition of Chromosome 21 Open Reading Frame 93 (C21orf93, Accession NM_145179). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf93. Cyclin M1 (CNNM1, Accession NM_020348) is another VGAM1214 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21607, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43451] Another function of VGAM1214 is therefore inhibition of

Cyclin M1 (CNNM1, Accession NM_020348). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. DKFZP434H132 (Accession XM_057020) is another VGAM1214 host target gene. DKFZP434H132 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434H132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H132 BINDING SITE, designated SEQ ID:36447, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43452] Another function of VGAM1214 is therefore inhibition of DKFZP434H132 (Accession XM_057020). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H132. DKFZP434I216 (Accession XM_085381) is another VGAM1214 host target gene. DKFZP434I216 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434I216, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I216 BINDING SITE, designated SEQ ID:38100, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43453] Another function of VGAM1214 is therefore inhibition of DKFZP434I216 (Accession XM_085381). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I216. DKFZP586G1122 (Accession XM_028643) is another VGAM1214 host target gene. DKFZP586G1122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586G1122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586G1122 BINDING SITE, designated SEQ ID:30726, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43454] Another function of VGAM1214 is therefore inhibition of DKFZP586G1122 (Accession XM_028643). Accordingly,

utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586G1122. DKFZP761E2110 (Accession NM_030953) is another VGAM1214 host target gene. DKFZP761E2110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761E2110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761E2110 BINDING SITE, designated SEQ ID:25224, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43455] Another function of VGAM1214 is therefore inhibition of DKFZP761E2110 (Accession NM_030953). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761E2110. FLJ22746 (Accession NM_024785) is another VGAM1214 host target gene. FLJ22746 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22746, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ22746 BINDING SITE, designated SEQ ID:24164, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43456] Another function of VGAM1214 is therefore inhibition of FLJ22746 (Accession NM_024785). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22746. FLJ23022 (Accession NM_025051) is another VGAM1214 host target gene. FLJ23022 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23022 BINDING SITE, designated SEQ ID:24646, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43457] Another function of VGAM1214 is therefore inhibition of FLJ23022 (Accession NM_025051). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23022. FLJ23420 (Accession NM_025061) is another

VGAM1214 host target gene. FLJ23420 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23420 BINDING SITE, designated SEQ ID:24660, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43458] Another function of VGAM1214 is therefore inhibition of FLJ23420 (Accession NM_025061). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23420. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_006625) is another VGAM1214 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:13410, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3925.

[43459] Another function of VGAM1214 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_006625). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. KIAA0152 (Accession NM_014730) is another VGAM1214 host target gene. KIAA0152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0152 BINDING SITE, designated SEQ ID:16340, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43460] Another function of VGAM1214 is therefore inhibition of KIAA0152 (Accession NM_014730). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0152. KIAA0930 (Accession XM_047214) is another VGAM1214 host target gene. KIAA0930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0930 BINDING SITE, designated SEQ ID:34916, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43461] Another function of VGAM1214 is therefore inhibition of KIAA0930 (Accession XM_047214). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0930. KIAA1029 (Accession NM_007286) is another VGAM1214 host target gene. KIAA1029 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1029 BINDING SITE, designated SEQ ID:14143, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43462] Another function of VGAM1214 is therefore inhibition of KIAA1029 (Accession NM_007286). Accordingly, utilities

of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1029. KIAA1157 (Accession XM_051093) is another VGAM1214 host target gene. KIAA1157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1157 BINDING SITE, designated SEQ ID:35749, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43463] Another function of VGAM1214 is therefore inhibition of KIAA1157 (Accession XM_051093). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1157. KIAA1602 (Accession XM_035497) is another VGAM1214 host target gene. KIAA1602 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1602 BINDING SITE, designated SEQ ID:32277, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43464] Another function of VGAM1214 is therefore inhibition of KIAA1602 (Accession XM_035497). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1602. KIAA1656 (Accession XM_038022) is another VGAM1214 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32736, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43465] Another function of VGAM1214 is therefore inhibition of KIAA1656 (Accession XM_038022). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1656. KIAA1854 (Accession XM_049884) is another VGAM1214 host target gene. KIAA1854 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35526, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43466] Another function of VGAM1214 is therefore inhibition of KIAA1854 (Accession XM_049884). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. Mitogen-activated Protein Kinase 8 Interacting Protein 3 (MAPK8IP3, Accession NM_033392) is another VGAM1214 host target gene. MAPK8IP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAPK8IP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK8IP3 BINDING SITE, designated SEQ ID:27218, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43467] Another function of VGAM1214 is therefore inhibition of Mitogen-activated Protein Kinase 8 Interacting Protein 3 (MAPK8IP3, Accession NM_033392). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK8IP3. Mesoderm Development Candidate 2 (MESDC2, Accession XM_051854) is another VGAM1214 host target gene. MESDC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MESDC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MESDC2 BINDING SITE, designated SEQ ID:35891, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43468] Another function of VGAM1214 is therefore inhibition of Mesoderm Development Candidate 2 (MESDC2, Accession XM_051854). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MESDC2. MSE55 (Accession NM_007061) is another VGAM1214 host target gene. MSE55 BINDING SITE is HOST TARGET binding site found

in the 5` untranslated region of mRNA encoded by MSE55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSE55 BINDING SITE, designated SEQ ID:13924, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43469] Another function of VGAM1214 is therefore inhibition of MSE55 (Accession NM_007061). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSE55. N4BP3 (Accession XM_038920) is another VGAM1214 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32931, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43470] Another function of VGAM1214 is therefore inhibition of

N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. PRIC285 (Accession XM_028918) is another VGAM1214 host target gene. PRIC285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRIC285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRIC285 BINDING SITE, designated SEQ ID:30802, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43471] Another function of VGAM1214 is therefore inhibition of PRIC285 (Accession XM_028918). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRIC285. RASD Family, Member 2 (RASD2, Accession NM_014310) is another VGAM1214 host target gene. RASD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RASD2 BINDING SITE, designated SEQ ID:15601, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43472] Another function of VGAM1214 is therefore inhibition of RASD Family, Member 2 (RASD2, Accession NM_014310). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASD2. Transmembrane 4 Superfamily Member 11 (plasmolipin) (TM4SF11, Accession NM_015993) is another VGAM1214 host target gene. TM4SF11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TM4SF11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TM4SF11 BINDING SITE, designated SEQ ID:18085, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43473] Another function of VGAM1214 is therefore inhibition of Transmembrane 4 Superfamily Member 11 (plasmolipin)

(TM4SF11, Accession NM_015993). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TM4SF11. Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037) is another VGAM1214 host target gene. TNRC9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TNRC9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC9 BINDING SITE, designated SEQ ID:35321, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43474] Another function of VGAM1214 is therefore inhibition of Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC9. ZNF340 (Accession XM_097701) is another VGAM1214 host target gene. ZNF340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF340, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF340 BINDING SITE, designated SEQ ID:41032, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43475] Another function of VGAM1214 is therefore inhibition of ZNF340 (Accession XM_097701). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF340. LOC127281 (Accession XM_059128) is another VGAM1214 host target gene. LOC127281 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127281 BINDING SITE, designated SEQ ID:36890, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43476] Another function of VGAM1214 is therefore inhibition of LOC127281 (Accession XM_059128). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC127281. LOC143153 (Accession XM_084440) is another VGAM1214 host target gene. LOC143153 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143153 BINDING SITE, designated SEQ ID:37581, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43477] Another function of VGAM1214 is therefore inhibition of LOC143153 (Accession XM_084440). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143153. LOC143196 (Accession XM_096389) is another VGAM1214 host target gene. LOC143196 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143196 BINDING SITE, designated SEQ ID:40330, to

the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43478] Another function of VGAM1214 is therefore inhibition of LOC143196 (Accession XM_096389). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143196. LOC144600 (Accession XM_096639) is another VGAM1214 host target gene. LOC144600 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144600 BINDING SITE, designated SEQ ID:40448, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43479] Another function of VGAM1214 is therefore inhibition of LOC144600 (Accession XM_096639). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144600. LOC147093 (Accession XM_097184) is another VGAM1214 host target gene. LOC147093 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC147093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147093 BINDING SITE, designated SEQ ID:40800, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43480] Another function of VGAM1214 is therefore inhibition of LOC147093 (Accession XM_097184). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147093. LOC149566 (Accession XM_097670) is another VGAM1214 host target gene. LOC149566 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149566 BINDING SITE, designated SEQ ID:41015, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43481] Another function of VGAM1214 is therefore inhibition of LOC149566 (Accession XM_097670). Accordingly, utilities

of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149566. LOC151171 (Accession XM_087116) is another VGAM1214 host target gene. LOC151171 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151171 BINDING SITE, designated SEQ ID:39066, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43482] Another function of VGAM1214 is therefore inhibition of LOC151171 (Accession XM_087116). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151171. LOC163682 (Accession XM_099402) is another VGAM1214 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC163682 BINDING SITE, designated SEQ ID:42098, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43483] Another function of VGAM1214 is therefore inhibition of LOC163682 (Accession XM_099402). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. LOC164714 (Accession XM_104657) is another VGAM1214 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42183, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43484] Another function of VGAM1214 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC203260 (Accession XM_114661) is another VGAM1214 host target gene. LOC203260 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203260 BINDING SITE, designated SEQ ID:43023, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43485] Another function of VGAM1214 is therefore inhibition of LOC203260 (Accession XM_114661). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203260. LOC204254 (Accession XM_118581) is another VGAM1214 host target gene. LOC204254 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204254 BINDING SITE, designated SEQ ID:43582, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43486] Another function of VGAM1214 is therefore inhibition of

LOC204254 (Accession XM_118581). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204254. LOC205095 (Accession XM_119820) is another VGAM1214 host target gene. LOC205095 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC205095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205095 BINDING SITE, designated SEQ ID:43602, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43487] Another function of VGAM1214 is therefore inhibition of LOC205095 (Accession XM_119820). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205095. LOC254617 (Accession XM_173236) is another VGAM1214 host target gene. LOC254617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC254617 BINDING SITE, designated SEQ ID:46518, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43488] Another function of VGAM1214 is therefore inhibition of LOC254617 (Accession XM_173236). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254617. LOC255299 (Accession XM_173564) is another VGAM1214 host target gene. LOC255299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255299 BINDING SITE, designated SEQ ID:46547, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43489] Another function of VGAM1214 is therefore inhibition of LOC255299 (Accession XM_173564). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255299. LOC256946 (Accession XM_170543) is an-

other VGAM1214 host target gene. LOC256946 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256946 BINDING SITE, designated SEQ ID:45360, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43490] Another function of VGAM1214 is therefore inhibition of LOC256946 (Accession XM_170543). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256946. LOC51152 (Accession NM_016181) is another VGAM1214 host target gene. LOC51152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51152 BINDING SITE, designated SEQ ID:18283, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43491] Another function of VGAM1214 is therefore inhibition of LOC51152 (Accession NM_016181). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51152. LOC91963 (Accession XM_041902) is another VGAM1214 host target gene. LOC91963 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91963 BINDING SITE, designated SEQ ID:33626, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43492] Another function of VGAM1214 is therefore inhibition of LOC91963 (Accession XM_041902). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91963. LOC92230 (Accession XM_043733) is another VGAM1214 host target gene. LOC92230 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92230, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92230 BINDING SITE, designated SEQ ID:34006, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43493] Another function of VGAM1214 is therefore inhibition of LOC92230 (Accession XM_043733). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92230. LOC93259 (Accession XM_050105) is another VGAM1214 host target gene. LOC93259 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93259 BINDING SITE, designated SEQ ID:35560, to the nucleotide sequence of VGAM1214 RNA, herein designated VGAM RNA, also designated SEQ ID:3925.

[43494] Another function of VGAM1214 is therefore inhibition of LOC93259 (Accession XM_050105). Accordingly, utilities of VGAM1214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC93259. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1215 (VGAM1215) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43495] VGAM1215 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1215 was detected is described hereinabove with reference to Figs. 1–8.

[43496] VGAM1215 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43497] VGAM1215 gene encodes a VGAM1215 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1215 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1215 precursor RNA is designated SEQ ID:1201, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1201 is located at position 188394 relative to the genome of Tupaia Herpesvirus.

- [43498] VGAM1215 precursor RNA folds onto itself, forming VGAM1215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43499] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1215 folded precursor RNA into VGAM1215 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM1215 RNA is designated SEQ ID:3926, and is provided hereinbelow with reference to the sequence listing part.

[43500] VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1215 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[43501] VGAM1215 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1215 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1215 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43502] The complementary binding of VGAM1215 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1215 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1215 host target RNA into VGAM1215 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43503] It is appreciated that VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1215 host target genes. The mRNA of each one of this plurality of VGAM1215 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1215 RNA, herein designated VGAM RNA, and which when bound by VGAM1215 RNA causes

inhibition of translation of respective one or more VGAM1215 host target proteins.

[43504] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1215 gene, herein designated VGAM GENE, on one or more VGAM1215 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43505] It is yet further appreciated that a function of VGAM1215 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1215 include diagnosis, prevention and

treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1215 correlate with, and may be deduced from, the identity of the host target genes which VGAM1215 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43506] Nucleotide sequences of the VGAM1215 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1215 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1215 are further described hereinbelow with reference to Table 1.

[43507] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1215 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1215 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43508] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1215 gene, herein designated VGAM is inhibition of expression of VGAM1215 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1215 correlate with, and may be deduced from, the identity of the target genes which VGAM1215 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43509] Fibromodulin (FMOD, Accession NM_002023) is a VGAM1215 host target gene. FMOD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMOD BINDING SITE, designated SEQ ID:7771, to the nucleotide sequence of VGAM1215 RNA, herein designated VGAM RNA, also designated SEQ ID:3926.

[43510] A function of VGAM1215 is therefore inhibition of Fibromodulin (FMOD, Accession NM_002023), a gene which affects the rate of fibrils formation. Accordingly, utilities of VGAM1215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMOD. The function of FMOD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM39.NDRG Family Member 3 (NDRG3, Accession NM_022477) is another VGAM1215 host target gene. NDRG3 BINDING SITE1 and NDRG3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG3 BINDING SITE1 and NDRG3 BINDING SITE2, designated SEQ ID:22846 and SEQ ID:25722 respectively, to the nucleotide sequence of VGAM1215 RNA, herein designated VGAM RNA, also designated SEQ ID:3926.

[43511] Another function of VGAM1215 is therefore inhibition of NDRG Family Member 3 (NDRG3, Accession NM_022477). Accordingly, utilities of VGAM1215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG3. RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733) is another VGAM1215 host target gene. RAB40A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB40A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of RAB40A BINDING SITE, designated SEQ ID:39931, to the nucleotide sequence of VGAM1215 RNA, herein designated VGAM RNA, also designated SEQ ID:3926.

[43512] Another function of VGAM1215 is therefore inhibition of RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733). Accordingly, utilities of VGAM1215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40A. LOC150150 (Accession XM_097820) is another VGAM1215 host target gene. LOC150150 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150150 BINDING SITE, designated SEQ ID:41134, to the nucleotide sequence of VGAM1215 RNA, herein designated VGAM RNA, also designated SEQ ID:3926.

[43513] Another function of VGAM1215 is therefore inhibition of LOC150150 (Accession XM_097820). Accordingly, utilities of VGAM1215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150150. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1216 (VGAM1216) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43514] VGAM1216 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1216 was detected is described hereinabove with reference to Figs. 1–8.

[43515] VGAM1216 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus. VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43516] VGAM1216 gene encodes a VGAM1216 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1216 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1216 precursor RNA is designated SEQ ID:1202, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1202 is located at position 190154 relative to the genome of Tupaia Herpesvirus.

- [43517] VGAM1216 precursor RNA folds onto itself, forming VGAM1216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43518] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1216 folded precursor RNA into VGAM1216 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM1216 RNA is designated SEQ ID:3927, and is provided hereinbelow with reference to the sequence listing part.

[43519] VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1216 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43520] VGAM1216 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1216 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1216 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43521] The complementary binding of VGAM1216 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1216 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1216 host target RNA into VGAM1216 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43522] It is appreciated that VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1216 host target genes. The mRNA of each one of this plurality of VGAM1216 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1216 RNA, herein designated VGAM RNA, and which when bound by VGAM1216 RNA causes

inhibition of translation of respective one or more VGAM1216 host target proteins.

[43523] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1216 gene, herein designated VGAM GENE, on one or more VGAM1216 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43524] It is yet further appreciated that a function of VGAM1216 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1216 include diagnosis, prevention and

treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1216 correlate with, and may be deduced from, the identity of the host target genes which VGAM1216 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43525] Nucleotide sequences of the VGAM1216 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1216 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1216 are further described hereinbelow with reference to Table 1.

[43526] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1216 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1216 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43527] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1216 gene, herein designated VGAM is inhibition of expression of VGAM1216 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1216 correlate with, and may be deduced from, the identity of the target genes which VGAM1216 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43528] Attractin (ATRN, Accession NM_139321) is a VGAM1216 host target gene. ATRN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRN BINDING SITE, designated SEQ ID:29302, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43529] A function of VGAM1216 is therefore inhibition of Attractin (ATRN, Accession NM_139321), a gene which is involved in the initial immune cell clustering during inflammatory response. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRN. The function of ATRN and its association with various diseases and clinical conditions, has been established by previous studies, as

described hereinabove with reference to

VGAM53.UDP-Gal:betaGlcNAc Beta

1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_033173) is another VGAM1216 host target gene. B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5, designated SEQ ID:27038, SEQ ID:27023, SEQ ID:27028, SEQ ID:27033 and SEQ ID:12700 respectively, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43530] Another function of VGAM1216 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_033173). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT5. Chromosome Condensation 1-like (CHC1L, Accession NM_001268) is another VGAM1216 host target gene. CHC1L BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by CHC1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHC1L BINDING SITE, designated SEQ ID:6929, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43531] Another function of VGAM1216 is therefore inhibition of Chromosome Condensation 1-like (CHC1L, Accession NM_001268). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHC1L. Cystinosis, Nephropathic (CTNS, Accession NM_004937) is another VGAM1216 host target gene. CTNS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CTNS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNS BINDING SITE, designated SEQ ID:11385, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43532] Another function of VGAM1216 is therefore inhibition of Cystinosis, Nephropathic (CTNS, Accession NM_004937). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNS. Cytochrome P450, Subfamily IIIA, Polypeptide 43 (CYP3A43, Accession NM_057096) is another VGAM1216 host target gene. CYP3A43 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP3A43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP3A43 BINDING SITE, designated SEQ ID:27663, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43533] Another function of VGAM1216 is therefore inhibition of Cytochrome P450, Subfamily IIIA, Polypeptide 43 (CYP3A43, Accession NM_057096), a gene which may be involved in the metabolism of insect hormones and in the breakdown of synthetic insecticides. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP3A43. The function of CYP3A43 has been established

by previous studies. By use of PCR on liver cDNA and 3-prime RACE, Domanski et al. (2001) isolated a cDNA encoding CYP3A43, a novel cytochrome P450 IIIA isoform. Sequence analysis predicted that the 503-amino acid protein differs from the other forms at the N terminus as well as at 2 C-terminal conserved sites and 4 sites that are important for the regioselectivity of steroid hydroxylation. RNA dot-blot analysis detected only weak expression in liver, whereas PCR of cDNA panels found expression in liver, kidney, pancreas, and prostate as well as fetal liver and fetal skeletal muscle. SDS-PAGE and Western blot analysis showed expression of an approximately 55-kD protein. Functional analysis indicated that, under appropriate conditions, CYP3A43 exhibits low but reproducible testosterone 6-beta-hydroxylase activity. Gellner et al. (2001) found the highest expression level of CYP3A43 mRNA in prostate, an organ with extensive steroid metabolism. It was also expressed in several other tissues including liver, where it could be induced by rifampicin. By EST database searching and 5-prime RACE, Westlind et al. (2001) also obtained a cDNA encoding CYP3A43. The deduced protein is 76%, 76%, and 72% identical to CYP3A4, CYP3A5, and CYP3A7, respectively. Real-time PCR in 10

different livers revealed that CYP3A43 is expressed at 0.1% and 2% of the levels of CYP3A4 and CYP3A5.

[43534] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43535] Gellner, K.; Eiselt, R.; Hustert, E.; Arnold, H.; Koch, I.; Haberl, M.; Deglmann, C. J.; Burk, O.; Buntefuss, D.; Escher, S.; Bishop, C.; Koebe, H.-G.; Brinkmann, U.; Klenk, H.-P.; Kleine, K.; Meyer, U. A.; Wojnowski, L. : Genomic organization of the human CYP3A locus: identification of a new, inducible CYP3A gene. *Pharmacogenetics* 11: 111-121, 2001. ; and

[43536] Westlind, A.; Malmebo, S.; Johansson, I.; Otter, C.; Andersson, T. B.; Ingelman-Sundberg, M.; Oscarson, M. : Cloning and tissue distribution of a novel human cytochrome P450 of the CYP3.

[43537] Further studies establishing the function and utilities of CYP3A43 are found in John Hopkins OMIM database record ID 606534, and in cited publications numbered 6463-6465 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dystrobrevin, Alpha (DTNA, Accession NM_001391) is another VGAM1216 host target gene. DTNA BINDING

SITE1 through DTNA BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DTNA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTNA BINDING SITE1 through DTNA BINDING SITE4, designated SEQ ID:7084, SEQ ID:26841, SEQ ID:26851 and SEQ ID:26846 respectively, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43538] Another function of VGAM1216 is therefore inhibition of Dystrobrevin, Alpha (DTNA, Accession NM_001391), a gene which may be involved in the formation and stability of synapses. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DTNA. The function of DTNA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1021. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is another VGAM1216 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7738, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43539] Another function of VGAM1216 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF2. The function of FGF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990) is another VGAM1216 host target gene. GABRE BINDING SITE1 through GABRE BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GABRE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of GABRE BINDING SITE1 through GABRE BINDING SITE4, designated SEQ ID:22533, SEQ ID:22511, SEQ ID:22515 and SEQ ID:11409 respectively, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43540] Another function of VGAM1216 is therefore inhibition of Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990), a gene which mediates neuronal inhibition by binding to the gaba/benzodiazepine receptor and opening an integral chloride channel. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABRE. The function of GABRE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259.Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFB3, Accession NM_003243) is another VGAM1216 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TGFBR3 BINDING SITE, designated SEQ ID:9249, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43541] Another function of VGAM1216 is therefore inhibition of Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFBR3, Accession NM_003243), a gene which involves in capturing and retaining TGF-beta for presentation to the signaling receptors. Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR3. The function of TGFBR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM139. Adenylate Kinase 5 (AK5, Accession NM_012093) is another VGAM1216 host target gene. AK5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK5 BINDING SITE, designated SEQ ID:14395, to the nucleotide sequence of VGAM1216 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3927.

[43542] Another function of VGAM1216 is therefore inhibition of Adenylate Kinase 5 (AK5, Accession NM_012093). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK5. Basic Helix-loop-helix Domain Containing, Class B, 2 (BHLHB2, Accession NM_003670) is another VGAM1216 host target gene. BHLHB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHLHB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHLHB2 BINDING SITE, designated SEQ ID:9755, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43543] Another function of VGAM1216 is therefore inhibition of Basic Helix-loop-helix Domain Containing, Class B, 2 (BHLHB2, Accession NM_003670). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHLHB2. Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749) is another VGAM1216

host target gene. C20orf139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf139 BINDING SITE, designated SEQ ID:41108, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43544] Another function of VGAM1216 is therefore inhibition of Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf139. FLJ13782 (Accession NM_024915) is another VGAM1216 host target gene. FLJ13782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13782 BINDING SITE, designated SEQ ID:24435, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM

RNA, also designated SEQ ID:3927.

[43545] Another function of VGAM1216 is therefore inhibition of FLJ13782 (Accession NM_024915). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13782. FLJ20151 (Accession NM_017689) is another VGAM1216 host target gene. FLJ20151 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20151, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20151 BINDING SITE, designated SEQ ID:19245, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43546] Another function of VGAM1216 is therefore inhibition of FLJ20151 (Accession NM_017689). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20151. FLJ22329 (Accession NM_024656) is another VGAM1216 host target gene. FLJ22329 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22329, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22329 BINDING SITE, designated SEQ ID:23959, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43547] Another function of VGAM1216 is therefore inhibition of FLJ22329 (Accession NM_024656). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22329. HTCD37 (Accession XM_041884) is another VGAM1216 host target gene. HTCD37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTCD37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTCD37 BINDING SITE, designated SEQ ID:33619, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43548] Another function of VGAM1216 is therefore inhibition of HTCD37 (Accession XM_041884). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with HTCD37. KIAA0295 (Accession XM_042833) is another VGAM1216 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33784, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43549] Another function of VGAM1216 is therefore inhibition of KIAA0295 (Accession XM_042833). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. KIAA0483 (Accession NM_015176) is another VGAM1216 host target gene. KIAA0483 BINDING SITE1 and KIAA0483 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0483, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0483 BINDING SITE1 and KIAA0483

BINDING SITE2, designated SEQ ID:17529 and SEQ ID:17527 respectively, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43550] Another function of VGAM1216 is therefore inhibition of KIAA0483 (Accession NM_015176). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0483. KIAA0934 (Accession XM_034536) is another VGAM1216 host target gene. KIAA0934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0934 BINDING SITE, designated SEQ ID:32120, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43551] Another function of VGAM1216 is therefore inhibition of KIAA0934 (Accession XM_034536). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0934. KIAA1522 (Accession XM_036299) is another

VGAM1216 host target gene. KIAA1522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1522 BINDING SITE, designated SEQ ID:32416, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43552] Another function of VGAM1216 is therefore inhibition of KIAA1522 (Accession XM_036299). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1522. KIAA1530 (Accession XM_042661) is another VGAM1216 host target gene. KIAA1530 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1530, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1530 BINDING SITE, designated SEQ ID:33731, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43553] Another function of VGAM1216 is therefore inhibition of KIAA1530 (Accession XM_042661). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1530. KIAA1908 (Accession XM_055834) is another VGAM1216 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36332, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43554] Another function of VGAM1216 is therefore inhibition of KIAA1908 (Accession XM_055834). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. MKP-7 (Accession XM_039106) is another VGAM1216 host target gene. MKP-7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKP-7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKP-7 BINDING SITE, designated SEQ ID:33005, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43555] Another function of VGAM1216 is therefore inhibition of MKP-7 (Accession XM_039106). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKP-7. Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540) is another VGAM1216 host target gene. NCOA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCOA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA2 BINDING SITE, designated SEQ ID:13296, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43556] Another function of VGAM1216 is therefore inhibition of Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540). Accordingly, utilities of VGAM1216 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA2. Protein Kinase C and Casein Kinase Substrate In Neurons 2 (PACSIN2, Accession NM_007229) is another VGAM1216 host target gene. PACSIN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACSIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN2 BINDING SITE, designated SEQ ID:14098, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43557] Another function of VGAM1216 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 2 (PACSIN2, Accession NM_007229). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN2. Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM_170929) is another VGAM1216 host target gene. PDE4DIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4DIP, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4DIP BINDING SITE, designated SEQ ID:45709, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43558] Another function of VGAM1216 is therefore inhibition of Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM_170929). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4DIP. Serine Hydrolase-like (SERHL, Accession XM_170987) is another VGAM1216 host target gene. SERHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERHL BINDING SITE, designated SEQ ID:45758, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43559] Another function of VGAM1216 is therefore inhibition of

Serine Hydrolase-like (SERHL, Accession XM_170987). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERHL. UMP-CMPK (Accession NM_016308) is another VGAM1216 host target gene. UMP-CMPK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UMP-CMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UMP-CMPK BINDING SITE, designated SEQ ID:18428, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43560] Another function of VGAM1216 is therefore inhibition of UMP-CMPK (Accession NM_016308). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UMP-CMPK. Ubiquitin Specific Protease 22 (USP22, Accession XM_042698) is another VGAM1216 host target gene. USP22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP22, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP22 BINDING SITE, designated SEQ ID:33753, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43561] Another function of VGAM1216 is therefore inhibition of Ubiquitin Specific Protease 22 (USP22, Accession XM_042698). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP22. LOC128954 (Accession XM_066252) is another VGAM1216 host target gene. LOC128954 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC128954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128954 BINDING SITE, designated SEQ ID:37321, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43562] Another function of VGAM1216 is therefore inhibition of LOC128954 (Accession XM_066252). Accordingly, utilities

of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128954. LOC133926 (Accession XM_059674) is another VGAM1216 host target gene. LOC133926 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133926 BINDING SITE, designated SEQ ID:37060, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43563] Another function of VGAM1216 is therefore inhibition of LOC133926 (Accession XM_059674). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133926. LOC146756 (Accession XM_097085) is another VGAM1216 host target gene. LOC146756 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC146756 BINDING SITE, designated SEQ ID:40734, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43564] Another function of VGAM1216 is therefore inhibition of LOC146756 (Accession XM_097085). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146756. LOC147632 (Accession NM_138478) is another VGAM1216 host target gene. LOC147632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147632 BINDING SITE, designated SEQ ID:28827, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43565] Another function of VGAM1216 is therefore inhibition of LOC147632 (Accession NM_138478). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147632. LOC152343 (Accession XM_087441) is another VGAM1216 host target gene. LOC152343 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152343 BINDING SITE, designated SEQ ID:39263, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43566] Another function of VGAM1216 is therefore inhibition of LOC152343 (Accession XM_087441). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152343. LOC220514 (Accession XM_017498) is another VGAM1216 host target gene. LOC220514 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220514 BINDING SITE, designated SEQ ID:30322, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43567] Another function of VGAM1216 is therefore inhibition of

LOC220514 (Accession XM_017498). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220514. LOC254015 (Accession XM_172977) is another VGAM1216 host target gene. LOC254015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254015 BINDING SITE, designated SEQ ID:46242, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43568] Another function of VGAM1216 is therefore inhibition of LOC254015 (Accession XM_172977). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254015. LOC257464 (Accession XM_116972) is another VGAM1216 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43169, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43569] Another function of VGAM1216 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC91813 (Accession XM_040862) is another VGAM1216 host target gene. LOC91813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE, designated SEQ ID:33398, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43570] Another function of VGAM1216 is therefore inhibition of LOC91813 (Accession XM_040862). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91813. LOC92181 (Accession XM_043394) is another

VGAM1216 host target gene. LOC92181 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92181 BINDING SITE, designated SEQ ID:33944, to the nucleotide sequence of VGAM1216 RNA, herein designated VGAM RNA, also designated SEQ ID:3927.

[43571] Another function of VGAM1216 is therefore inhibition of LOC92181 (Accession XM_043394). Accordingly, utilities of VGAM1216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92181. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1217 (VGAM1217) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43572] VGAM1217 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1217 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[43573] VGAM1217 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tupaia Herpesvirus.

VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43574] VGAM1217 gene encodes a VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1217 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1217 precursor RNA is designated SEQ ID:1203, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1203 is located at position 190840 relative to the genome of Tupaia Herpesvirus.

[43575] VGAM1217 precursor RNA folds onto itself, forming VGAM1217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43576] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1217 folded precursor RNA into VGAM1217 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1217 RNA is designated SEQ ID:3928, and is provided hereinbelow with reference to the sequence listing part.

[43577] VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1217 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43578] VGAM1217 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1217 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1217 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1217 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43579] The complementary binding of VGAM1217 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1217 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1217 host target RNA into VGAM1217 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43580] It is appreciated that VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1217 host target genes. The mRNA of each one of this plurality of VGAM1217 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1217 RNA, herein designated VGAM RNA, and which when bound by VGAM1217 RNA causes inhibition of translation of respective one or more VGAM1217 host target proteins.

[43581] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1217 gene, herein designated VGAM GENE, on one or more VGAM1217 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43582] It is yet further appreciated that a function of VGAM1217 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGAM1217 correlate with, and may be deduced from, the identity of the host target genes which VGAM1217 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43583] Nucleotide sequences of the VGAM1217 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1217 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1217 are further described hereinbelow with reference to Table 1.

[43584] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1217 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1217 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43585] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1217 gene, herein designated VGAM is inhibition of expression of VGAM1217 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1217 correlate with, and may be deduced from, the identity of the target genes which VGAM1217 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43586] V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_005157) is a VGAM1217 host target gene. ABL1 BINDING SITE1 and ABL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABL1, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABL1 BINDING SITE1 and ABL1 BINDING SITE2, designated SEQ ID:11637 and SEQ ID:14226 respectively, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43587] A function of VGAM1217 is therefore inhibition of V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_005157). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABL1. Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM_014586) is another VGAM1217 host target gene. HUNK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HUNK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HUNK BINDING SITE, designated SEQ ID:15951, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43588] Another function of VGAM1217 is therefore inhibition of

Hormonally Upregulated Neu-associated Kinase (HUNK, Accession NM_014586). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HUNK. Insulin-like Growth Factor Binding Protein 3 (IGFBP3, Accession NM_000598) is another VGAM1217 host target gene. IGFBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGFBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGFBP3 BINDING SITE, designated SEQ ID:6197, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43589] Another function of VGAM1217 is therefore inhibition of Insulin-like Growth Factor Binding Protein 3 (IGFBP3, Accession NM_000598). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGFBP3. Interleukin 10 Receptor, Alpha (IL10RA, Accession XM_006447) is another VGAM1217 host target gene. IL10RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by IL10RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL10RA BINDING SITE, designated SEQ ID:29999, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43590] Another function of VGAM1217 is therefore inhibition of Interleukin 10 Receptor, Alpha (IL10RA, Accession XM_006447), a gene which is a receptor for il-10. Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL10RA. The function of IL10RA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM134. Insulin Receptor Substrate 2 (IRS2, Accession XM_007095) is another VGAM1217 host target gene. IRS2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IRS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRS2 BINDING SITE, desig-

nated SEQ ID:30033, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43591] Another function of VGAM1217 is therefore inhibition of Insulin Receptor Substrate 2 (IRS2, Accession XM_007095), a gene which may mediate the control of various cellular processes by insulin. Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRS2. The function of IRS2 has been established by previous studies. The protein IRS1 (OMIM Ref. No. 147545) acts as an interface between signaling proteins with Src homology-2 domains (SH2 proteins) and the receptors for insulin (INS; 176730), IGF2 (OMIM Ref. No. 147470), growth hormone (GH1; 139250), several interleukins (IL4, 147780; IL9, 146931; IL13, 147683), and other cytokines. It regulates gene expression and stimulates mitogenesis and appears to mediate insulin/IGF1-stimulated glucose transport. Thus, the finding that survival of the homozygous *Irs1* knockout mouse with only mild resistance to hypertension was surprising. This dilemma was provisionally resolved by the discovery by Sun et al. (1995) of a second IRS signaling protein in mouse. They purified and

cloned a likely candidate from mouse myeloid progenitor cells and, because of its resemblance to IRS1, they designated it IRS2. Alignment of the sequences of IRS2 and IRS1 demonstrated a highly conserved N terminus containing a pleckstrin-homology domain and a phosphotyrosine-binding (PTB) domain, and a poorly conserved C terminus containing several tyrosine phosphorylation motifs. IRS2 is expressed in many cells, including tissues from the homozygous IRS1 knockout mouse. Sun et al. (1995) suggested that IRS2 may be essential for signaling by several receptor systems. Mammarella et al. (2000) genotyped 193 Italian patients with type II diabetes (OMIM Ref. No. 125853) and 206 control subjects for the IRS2 G1057D polymorphism (600797.0001). They found evidence for a strong association between type II diabetes and the polymorphism, which appears to be protective against type II diabetes in a codominant fashion. Animal model experiments lend further support to the function of IRS2. Tobe et al. (2001) observed that *Irs2*-deficient mice (Kubota et al. (2000)) showed increased adiposity with increased serum leptin level, suggesting leptin resistance before the mice developed diabetes. Using oligonucleotide microarray and Northern blot analyses to analyze gene expres-

sion, Tobe et al. (2001) detected increased expression of SREBP1, a downstream target of insulin, in Irs2-deficient mouse liver. Using high dose leptin administration, They provided evidence that leptin resistance in Irs2-deficient mice is causally related to SREBP1 gene induction. The authors concluded that Irs2 gene disruption results in leptin resistance, causing SREBP1 gene induction, obesity, fatty liver, and diabetes

[43592] It is appreciated that the abovementioned animal model for IRS2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[43593] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43594] Sun, X. J.; Wang, L.-M.; Zhang, Y.; Yenush, L.; Myers, M. G., Jr.; Glasheen, E.; Lane, W. S.; Pierce, J. H.; White, M. F. : Role of IRS-2 in insulin and cytokine signalling. Nature 377: 173-177, 1995. ; and

[43595] Tobe, K.; Suzuki, R.; Aoyama, M.; Yamauchi, T.; Kamon, J.; Kubota, N.; Terauchi, Y.; Matsui, J.; Akanuma, Y.; Kimura, S.; Tanaka, J.; Abe, M.; Ohsumi, J.; Nagai, R.; Kadowaki, T. : Incre.

[43596] Further studies establishing the function and utilities of IRS2 are found in John Hopkins OMIM database record ID 600797, and in cited publications numbered 135, 1615–1617, 12223, 1085 and 12640–1620 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leucine Zipper Protein 1 (LUZP1, Accession NM_033631) is another VGAM1217 host target gene. LUZP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LUZP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LUZP1 BINDING SITE, designated SEQ ID:27352, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43597] Another function of VGAM1217 is therefore inhibition of Leucine Zipper Protein 1 (LUZP1, Accession NM_033631). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LUZP1. Mannose Receptor, C Type 1 (MRC1, Accession NM_002438) is another VGAM1217 host target gene. MRC1 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by MRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRC1 BINDING SITE, designated SEQ ID:8281, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43598] Another function of VGAM1217 is therefore inhibition of Mannose Receptor, C Type 1 (MRC1, Accession NM_002438), a gene which mediates the endocytosis of glycoproteins. Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRC1. The function of MRC1 has been established by previous studies. Recognition of complex carbohydrate structures plays an important role in a number of biologic processes, including cell-cell recognition, serum glycoprotein turnover, and neutralization of pathogens (Kim et al., 1992). Many of the endogenous animal lectins which mediate these recognition events share a common Ca^{2+} -dependent structural motif, which has been designated a C-type carbohydrate-recognition domain (CRD). The mannose receptor found

on macrophages and on endothelial cells of the liver is the only known example of a C-type lectin that contains multiple C-type CRDs. One function of the receptor is to bind high-mannose structures on the surface of potentially pathogenic viruses, bacteria, and fungi, so that they can be neutralized by phagocytic engulfment. Animal model experiments lend further support to the function of MRC1. Lee et al. (2002) generated mice genetically deficient in mannose receptor. MR $-/-$ mice were defective in clearing proteins bearing accessible mannose and N-acetylglucosamine residues and had elevated levels of 8 different lysosomal hydrolases. Proteomic analysis of MR $-/-$ and control mouse sera showed that an additional 4 out of 52 proteins identified were elevated in MR $-/-$ serum. Each of these proteins is upregulated during inflammation and wound healing. Thus, Lee et al. (2002) concluded that MR appears to operate as an essential regulator of serum glycoprotein homeostasis. The proteins upregulated during inflammation included C-terminal propeptide domains of the pro- α -1 and -2 chains of type I procollagen (120150 and 120160, respectively) and the pro- α -1 chain of type III procollagen (OMIM Ref. No. 120180), as well as fetuin-B (OMIM Ref. No. 605954).

Lee et al. (2002) demonstrated that the mannose receptor is required for rapid clearance of a subset of mannose-bearing serum glycoproteins that are normally elevated during inflammation, but it does not appear to regulate the initiation of inflammation.

[43599] It is appreciated that the abovementioned animal model for MRC1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[43600] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43601] Kim, S. J.; Ruiz, N.; Bezouska, K.; Drickamer, K. : Organization of the gene encoding the human macrophage mannose receptor (MRC1). *Genomics* 14: 721–727, 1992. ; and

[43602] Lee, S. J.; Evers, S.; Roeder, D.; Parlow, A. F.; Risteli, J.; Risteli, L.; Lee, Y. C.; Feizi, T.; Langen, H.; Nussenzweig, M. C. : Mannose receptor-mediated regulation of serum glycopr.

[43603] Further studies establishing the function and utilities of MRC1 are found in John Hopkins OMIM database record ID 153618, and in cited publications numbered

11538–11541 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 38 (ZNF38, Accession XM_170135) is another VGAM1217 host target gene. ZNF38 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF38 BINDING SITE, designated SEQ ID:45311, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43604] Another function of VGAM1217 is therefore inhibition of Zinc Finger Protein 38 (ZNF38, Accession XM_170135). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF38. Aminoadipate-semialdehyde Dehydrogenase-phosphopantetheinyl Transferase (AASDHPPT, Accession NM_015423) is another VGAM1217 host target gene. AASDHPPT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AASDHPPT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AASDHPPT BINDING SITE, designated SEQ ID:17725, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43605] Another function of VGAM1217 is therefore inhibition of Aminoadipate-semialdehyde Dehydrogenase-phosphopantetheinyl Transferase (AASDHPPT, Accession NM_015423). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AASDHPPT. Chromosome 20 Open Reading Frame 81 (C20orf81, Accession NM_022760) is another VGAM1217 host target gene. C20orf81 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf81, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf81 BINDING SITE, designated SEQ ID:23003, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43606] Another function of VGAM1217 is therefore inhibition of

Chromosome 20 Open Reading Frame 81 (C20orf81, Accession NM_022760). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf81. CDT1 (Accession XM_085327) is another VGAM1217 host target gene. CDT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDT1 BINDING SITE, designated SEQ ID:38065, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43607] Another function of VGAM1217 is therefore inhibition of CDT1 (Accession XM_085327). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDT1. DKFZP586A0522 (Accession NM_014033) is another VGAM1217 host target gene. DKFZP586A0522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586A0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZP586A0522 BINDING SITE, designated SEQ ID:15263, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43608] Another function of VGAM1217 is therefore inhibition of DKFZP586A0522 (Accession NM_014033). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586A0522. DKFZp586I021 (Accession NM_032271) is another VGAM1217 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26029, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43609] Another function of VGAM1217 is therefore inhibition of DKFZp586I021 (Accession NM_032271). Accordingly, utilities of VGAM1217 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp586I021. FLJ10261 (Accession NM_018043) is another VGAM1217 host target gene. FLJ10261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10261 BINDING SITE, designated SEQ ID:19788, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43610] Another function of VGAM1217 is therefore inhibition of FLJ10261 (Accession NM_018043). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10261. FLJ13855 (Accession NM_023079) is another VGAM1217 host target gene. FLJ13855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13855 BINDING SITE, designated SEQ ID:23344, to the nucleotide

sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43611] Another function of VGAM1217 is therefore inhibition of FLJ13855 (Accession NM_023079). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13855. FLJ14451 (Accession NM_032786) is another VGAM1217 host target gene. FLJ14451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14451 BINDING SITE, designated SEQ ID:26540, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43612] Another function of VGAM1217 is therefore inhibition of FLJ14451 (Accession NM_032786). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14451. Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424) is another VGAM1217 host target gene. HSPB7 BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by HSPB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPB7 BINDING SITE, designated SEQ ID:15783, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43613] Another function of VGAM1217 is therefore inhibition of Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPB7. KIAA0211 (Accession NM_014630) is another VGAM1217 host target gene. KIAA0211 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0211 BINDING SITE, designated SEQ ID:15993, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43614] Another function of VGAM1217 is therefore inhibition of KIAA0211 (Accession NM_014630). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0211. KIAA0546 (Accession XM_049055) is another VGAM1217 host target gene. KIAA0546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0546 BINDING SITE, designated SEQ ID:35333, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43615] Another function of VGAM1217 is therefore inhibition of KIAA0546 (Accession XM_049055). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0546. KIAA0710 (Accession NM_014871) is another VGAM1217 host target gene. KIAA0710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0710, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0710 BINDING SITE, designated SEQ ID:16993, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43616] Another function of VGAM1217 is therefore inhibition of KIAA0710 (Accession NM_014871). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0710. KIAA1045 (Accession XM_048592) is another VGAM1217 host target gene. KIAA1045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35205, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43617] Another function of VGAM1217 is therefore inhibition of KIAA1045 (Accession XM_048592). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1045. KIAA1423 (Accession XM_029703) is another VGAM1217 host target gene. KIAA1423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1423 BINDING SITE, designated SEQ ID:30922, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43618] Another function of VGAM1217 is therefore inhibition of KIAA1423 (Accession XM_029703). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1423. MGC2628 (Accession NM_024076) is another VGAM1217 host target gene. MGC2628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2628 BINDING SITE, designated SEQ ID:23507, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM

RNA, also designated SEQ ID:3928.

[43619] Another function of VGAM1217 is therefore inhibition of MGC2628 (Accession NM_024076). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2628. MGC3020 (Accession NM_024048) is another VGAM1217 host target gene. MGC3020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3020 BINDING SITE, designated SEQ ID:23484, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43620] Another function of VGAM1217 is therefore inhibition of MGC3020 (Accession NM_024048). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3020. MSP (Accession NM_032046) is another VGAM1217 host target gene. MSP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MSP, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSP BINDING SITE, designated SEQ ID:25761, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43621] Another function of VGAM1217 is therefore inhibition of MSP (Accession NM_032046). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSP. Ubiquitin Specific Protease 3 (USP3, Accession XM_116973) is another VGAM1217 host target gene. USP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by USP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP3 BINDING SITE, designated SEQ ID:43171, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43622] Another function of VGAM1217 is therefore inhibition of Ubiquitin Specific Protease 3 (USP3, Accession XM_116973). Accordingly, utilities of VGAM1217 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with USP3. LOC131873 (Accession XM_067585) is another VGAM1217 host target gene. LOC131873 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC131873, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131873 BINDING SITE, designated SEQ ID:37363, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43623] Another function of VGAM1217 is therefore inhibition of LOC131873 (Accession XM_067585). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131873. LOC145231 (Accession XM_096740) is another VGAM1217 host target gene. LOC145231 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145231 BINDING SITE, designated SEQ ID:40521, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43624] Another function of VGAM1217 is therefore inhibition of LOC145231 (Accession XM_096740). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145231. LOC146237 (Accession XM_096954) is another VGAM1217 host target gene. LOC146237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146237 BINDING SITE, designated SEQ ID:40670, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43625] Another function of VGAM1217 is therefore inhibition of LOC146237 (Accession XM_096954). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146237. LOC146713 (Accession XM_097071) is another VGAM1217 host target gene. LOC146713 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146713, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146713 BINDING SITE, designated SEQ ID:40717, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43626] Another function of VGAM1217 is therefore inhibition of LOC146713 (Accession XM_097071). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146713. LOC147664 (Accession XM_085826) is another VGAM1217 host target gene. LOC147664 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147664, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147664 BINDING SITE, designated SEQ ID:38351, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43627] Another function of VGAM1217 is therefore inhibition of

LOC147664 (Accession XM_085826). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147664. LOC151031 (Accession XM_103784) is another VGAM1217 host target gene. LOC151031 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151031 BINDING SITE, designated SEQ ID:42156, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43628] Another function of VGAM1217 is therefore inhibition of LOC151031 (Accession XM_103784). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151031. LOC166341 (Accession XM_093804) is another VGAM1217 host target gene. LOC166341 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC166341, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC166341 BINDING SITE, designated SEQ ID:40211, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43629] Another function of VGAM1217 is therefore inhibition of LOC166341 (Accession XM_093804). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166341. LOC196529 (Accession XM_113746) is another VGAM1217 host target gene. LOC196529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196529 BINDING SITE, designated SEQ ID:42410, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43630] Another function of VGAM1217 is therefore inhibition of LOC196529 (Accession XM_113746). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196529. LOC205313 (Accession XM_119628) is an-

other VGAM1217 host target gene. LOC205313 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205313 BINDING SITE, designated SEQ ID:43593, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43631] Another function of VGAM1217 is therefore inhibition of LOC205313 (Accession XM_119628). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205313. LOC253612 (Accession XM_172985) is another VGAM1217 host target gene. LOC253612 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253612 BINDING SITE, designated SEQ ID:46256, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43632] Another function of VGAM1217 is therefore inhibition of LOC253612 (Accession XM_172985). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253612. LOC256683 (Accession XM_172321) is another VGAM1217 host target gene. LOC256683 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256683, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256683 BINDING SITE, designated SEQ ID:46070, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43633] Another function of VGAM1217 is therefore inhibition of LOC256683 (Accession XM_172321). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256683. LOC90288 (Accession XM_030669) is another VGAM1217 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31111, to the nucleotide sequence of VGAM1217 RNA, herein designated VGAM RNA, also designated SEQ ID:3928.

[43634] Another function of VGAM1217 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities of VGAM1217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1218 (VGAM1218) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43635] VGAM1218 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1218 was detected is described hereinabove with reference to Figs. 1-8.

[43636] VGAM1218 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1218 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[43637] VGAM1218 gene encodes a VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1218 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1218 precursor RNA is designated SEQ ID:1204, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1204 is located at position 161690 relative to the genome of Fowlpox Virus.

[43638] VGAM1218 precursor RNA folds onto itself, forming VGAM1218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43639] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1218 folded precursor RNA into VGAM1218

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1218 RNA is designated SEQ ID:3929, and is provided hereinbelow with reference to the sequence listing part.

[43640] VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1218 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43641] VGAM1218 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1218 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1218 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43642] The complementary binding of VGAM1218 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1218 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1218 host target RNA into VGAM1218 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[43643] It is appreciated that VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1218 host target genes. The mRNA of each one of this plurality of VGAM1218 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1218 RNA, herein designated VGAM RNA, and which when bound by VGAM1218 RNA causes inhibition of translation of respective one or more VGAM1218 host target proteins.

[43644] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1218 gene, herein designated VGAM GENE, on one or more VGAM1218 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43645] It is yet further appreciated that a function of VGAM1218 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1218 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1218 correlate with, and may be deduced from, the identity of the host target genes which VGAM1218 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43646] Nucleotide sequences of the VGAM1218 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1218 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1218 are further described hereinbelow with reference to Table 1.

[43647] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1218 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1218 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43648] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1218 gene, herein designated VGAM is inhibition of expression of VGAM1218 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1218 correlate with, and may be deduced from, the identity of the target genes which VGAM1218 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43649] LOC124976 (Accession XM_058879) is a VGAM1218 host target gene. LOC124976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124976 BINDING SITE, designated SEQ ID:36780, to the nucleotide sequence of VGAM1218 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3929.

[43650] A function of VGAM1218 is therefore inhibition of LOC124976 (Accession XM_058879). Accordingly, utilities of VGAM1218 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124976. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1219 (VGAM1219) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43651] VGAM1219 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1219 was detected is described hereinabove with reference to Figs. 1–8.

[43652] VGAM1219 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43653] VGAM1219 gene encodes a VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1219 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1219 precursor RNA is designated SEQ ID:1205, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1205 is located at position 157189 relative to the genome of Fowlpox Virus.

- [43654] VGAM1219 precursor RNA folds onto itself, forming VGAM1219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43655] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1219 folded precursor RNA into VGAM1219 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1219 RNA is designated SEQ ID:3930, and is provided hereinbelow with reference to the sequence listing part.

[43656] VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1219 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43657] VGAM1219 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1219 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1219 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43658] The complementary binding of VGAM1219 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1219 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1219 host target RNA into VGAM1219 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43659] It is appreciated that VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1219 host target genes. The mRNA of

each one of this plurality of VGAM1219 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1219 RNA, herein designated VGAM RNA, and which when bound by VGAM1219 RNA causes inhibition of translation of respective one or more VGAM1219 host target proteins.

[43660] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1219 gene, herein designated VGAM GENE, on one or more VGAM1219 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[43661] It is yet further appreciated that a function of VGAM1219 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1219 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1219 correlate with, and may be deduced from, the identity of the host target genes which VGAM1219 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43662] Nucleotide sequences of the VGAM1219 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1219 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1219 are further described hereinbelow with reference to Table 1.

[43663] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1219 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1219 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43664] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1219 gene, herein designated VGAM is inhibition of expression of VGAM1219 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1219 correlate with, and may be deduced from, the identity of the target genes which VGAM1219 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43665] COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_078470) is a VGAM1219 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:27791, to the nucleotide sequence of VGAM1219 RNA, herein designated VGAM RNA, also designated SEQ ID:3930.

[43666] A function of VGAM1219 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast)

(COX15, Accession NM_078470). Accordingly, utilities of VGAM1219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Cytochrome P450, Subfamily XXXIX (oxysterol 7 alpha-hydroxylase), Polypeptide 1 (CYP39A1, Accession NM_016593) is another VGAM1219 host target gene. CYP39A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP39A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP39A1 BINDING SITE, designated SEQ ID:18681, to the nucleotide sequence of VGAM1219 RNA, herein designated VGAM RNA, also designated SEQ ID:3930.

[43667] Another function of VGAM1219 is therefore inhibition of Cytochrome P450, Subfamily XXXIX (oxysterol 7 alpha-hydroxylase), Polypeptide 1 (CYP39A1, Accession NM_016593). Accordingly, utilities of VGAM1219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP39A1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred

to here as Viral Genomic Address Messenger 1220 (VGAM1220) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43668] VGAM1220 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1220 was detected is described hereinabove with reference to Figs. 1–8.

[43669] VGAM1220 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43670] VGAM1220 gene encodes a VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1220 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1220 precursor RNA is designated SEQ ID:1206, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1206 is located at position 28289 relative to the genome of Fowl Adenovirus D.

[43671] VGAM1220 precursor RNA folds onto itself, forming VGAM1220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43672] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1220 folded precursor RNA into VGAM1220 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM1220 RNA is designated SEQ ID:3931, and is provided hereinbelow with reference to the sequence listing part.

[43673] VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1220 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1220 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43674] VGAM1220 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1220 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1220 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43675] The complementary binding of VGAM1220 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1220 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1220 host target RNA into VGAM1220 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43676] It is appreciated that VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1220 host target genes. The mRNA of each one of this plurality of VGAM1220 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1220 RNA, herein designated VGAM RNA, and which when bound by VGAM1220 RNA causes inhibition of translation of respective one or more VGAM1220 host target proteins.

[43677] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1220 gene, herein designated VGAM GENE, on one or more VGAM1220 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43678] It is yet further appreciated that a function of VGAM1220 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1220 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1220 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43679] Nucleotide sequences of the VGAM1220 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1220 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1220 are further described hereinbelow with reference to Table 1.

[43680] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1220 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1220 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43681] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1220 gene, herein designated VGAM is inhibition of expression of VGAM1220 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1220 correlate with, and may be deduced from, the identity of the target genes which VGAM1220

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43682] Chromosome 1 Open Reading Frame 1 (C1orf1, Accession NM_001213) is a VGAM1220 host target gene. C1orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf1 BINDING SITE, designated SEQ ID:6873, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43683] A function of VGAM1220 is therefore inhibition of Chromosome 1 Open Reading Frame 1 (C1orf1, Accession NM_001213). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf1. Cyclic Nucleotide Gated Channel Alpha 3 (CNGA3, Accession NM_001298) is another VGAM1220 host target gene. CNGA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNGA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of CNGA3 BINDING SITE, designated SEQ ID:6978, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43684] Another function of VGAM1220 is therefore inhibition of Cyclic Nucleotide Gated Channel Alpha 3 (CNGA3, Accession NM_001298). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNGA3. Cut-like 1, CCAAT Displacement Protein (Drosophila) (CUTL1, Accession NM_001913) is another VGAM1220 host target gene. CUTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUTL1 BINDING SITE, designated SEQ ID:7629, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43685] Another function of VGAM1220 is therefore inhibition of Cut-like 1, CCAAT Displacement Protein (Drosophila) (CUTL1, Accession NM_001913), a gene which may regulate gene expression, morphogenesis, and differentiation.

Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CUTL1. The function of CUTL1 has been established by previous studies. The activity of CDP, CCAAT displacement protein, was first identified in sea urchin as a possible repressor of a sperm-specific histone H2b gene. As implied by its name, CDP is thought to act by preventing binding of positively-acting CCAAT factors to promoters, although there is little experimental evidence for this (Neufeld, 1995). The wide distribution of CDP in mammalian cell lines and its postulated mechanism of action made it a potential candidate for a general repressor of developmentally regulated genes. Neufeld et al. (1992) purified CDP from HeLa cells by DNA binding-site affinity chromatography. The cDNA encoding CDP was obtained by immunoscreening a lambda-gt11 library with antibody raised against purified protein. The deduced primary amino acid sequence of CDP showed remarkable homology to the *Drosophila* homeoprotein cut with respect to the presence of a unique homeodomain and 'cut repeats.' As cut participates in determination of cell fate in several tissues in *Drosophila*, the similarity predicts a broad role for CDP in mammalian development. Neufeld et

al. (1992) studied CDP because of its likely role in regulation of the gene encoding the protein deficient in X-linked chronic granulomatous disease (OMIM Ref. No. 306400). Zeng et al. (1997) identified polymorphic markers within and directly adjacent to CUTL1 at 7q22 and demonstrated that these markers are present in a commonly deleted region in 7 of 50 uterine leiomyomas examined. Furthermore, Northern blot analysis revealed that CUTL1 mRNA levels were reduced in 8 of 13 tumors. Zeng et al. (1997) concluded that CUTL1 may act as a tumor suppressor gene whose inactivation could be of pathologic importance in the etiology of uterine leiomyomas.

[43686] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43687] Neufeld, E. J.; Skalnik, D. G.; Lievens, P. M.-J.; Orkin, S. H. : Human CCAAT displacement protein is homologous to the *Drosophila* homeoprotein, cut. *Nature Genet.* 1: 50-55, 1992. ; and

[43688] Snyder, S. R.; Wang, J.; Waring, J. F.; Ginder, G. D. : Identification of CCAAT displacement protein (CDP/cut) as a locus-specific repressor of major histocompatibility complex gene expr.

[43689] Further studies establishing the function and utilities of CUTL1 are found in John Hopkins OMIM database record ID 116896, and in cited publications numbered 4094–4099 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM_028642) is another VGAM1220 host target gene. ITGA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA5 BINDING SITE, designated SEQ ID:30723, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43690] Another function of VGAM1220 is therefore inhibition of Integrin, Alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5, Accession XM_028642), a gene which is receptor for fibronectin and fibrinogen and recognizes the sequence r–g–d in its ligands. Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA5.

The function of ITGA5 has been established by previous studies. The fibronectin receptor, a member of the integrin family of heterodimeric glycopeptides, mediates the binding of cells to fibronectin substrata. To study the structure of the receptor, Argraves et al. (1986) isolated cDNA clones coding for the alpha subunit from a placental cDNA library. The cDNAs code for 229 amino acids from the C-terminus of the alpha subunit. The deduced sequence had a hydrophobic region with properties characteristic of a membrane-spanning domain. Argraves et al. (1987) deduced the amino acid sequence from cDNA. The alpha subunit, which is processed into 2 polypeptides disulfide-bonded to one another, has 1,008 amino acids; the beta subunit has 778 amino acids. Fitzgerald et al. (1987) presented comparisons of the cDNA-derived protein sequences of fibronectin receptor, vitronectin receptor (OMIM Ref. No. 193210), and platelet glycoprotein IIb (OMIM Ref. No. 273800). Sosnoski et al. (1988) assigned the FNRA gene to 12q11-q13 by Southern analysis of somatic cell hybrid DNA. Location on chromosome 12 was confirmed by Spurr and Rooke (1991) by study of human/rodent somatic cell hybrids. Krissansen et al. (1992) pointed out the possible significance of the fact that a re-

lated gene coding for integrin beta-7 subunit (ITGB7; 147559) is also located on chromosome 12. Adkison et al. (1994) mapped the murine homolog, Itga5, to chromosome 15, distal to D15Mit16, by analysis of DNA from an interspecific backcross

[43691] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43692] Adkison, L. R.; White, R. A.; Haney, D. M.; Lee, J. C.; Pusey, K. T.; Gardner, J. : The fibronectin receptor, alpha subunit (Itga5) maps to murine chromosome 15, distal to D15Mit16. Mammalian Genome 5: 456-457, 1994. ; and

[43693] Argraves, W. S.; Pytela, R.; Suzuki, S.; Millan, J. L.; Pierschbacher, M. D.; Ruoslahti, E. : cDNA sequences from the alpha subunit of the fibronectin receptor predict a trans-membrane d.

[43694] Further studies establishing the function and utilities of ITGA5 are found in John Hopkins OMIM database record ID 135620, and in cited publications numbered 3333-3339 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nucleosome Assembly Protein 1-like 4 (NAP1L4, Accession NM_005969) is another VGAM1220 host target

gene. NAP1L4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAP1L4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAP1L4 BINDING SITE, designated SEQ ID:12590, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43695] Another function of VGAM1220 is therefore inhibition of Nucleosome Assembly Protein 1-like 4 (NAP1L4, Accession NM_005969), a gene which may have a role as a histone chaperone. Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAP1L4. The function of NAP1L4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Thrombomodulin (THBD, Accession NM_000361) is another VGAM1220 host target gene. THBD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by THBD, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBD BINDING SITE, designated SEQ ID:5919, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43696] Another function of VGAM1220 is therefore inhibition of Thrombomodulin (THBD, Accession NM_000361). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBD. IMPACT (Accession NM_018439) is another VGAM1220 host target gene. IMPACT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPACT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPACT BINDING SITE, designated SEQ ID:20500, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43697] Another function of VGAM1220 is therefore inhibition of IMPACT (Accession NM_018439). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IM-

PACT. KIAA0193 (Accession NM_014766) is another VGAM1220 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16544, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43698] Another function of VGAM1220 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. KIAA0476 (Accession NM_014856) is another VGAM1220 host target gene. KIAA0476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0476 BINDING SITE, designated SEQ ID:16905, to the nucleotide sequence of VGAM1220 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3931.

[43699] Another function of VGAM1220 is therefore inhibition of KIAA0476 (Accession NM_014856). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0476. KIAA1337 (Accession XM_052561) is another VGAM1220 host target gene. KIAA1337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1337 BINDING SITE, designated SEQ ID:35984, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43700] Another function of VGAM1220 is therefore inhibition of KIAA1337 (Accession XM_052561). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1337. MGC4415 (Accession NM_031484) is another VGAM1220 host target gene. MGC4415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4415, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4415 BINDING SITE, designated SEQ ID:25569, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43701] Another function of VGAM1220 is therefore inhibition of MGC4415 (Accession NM_031484). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4415. PI4KII (Accession NM_018425) is another VGAM1220 host target gene. PI4KII BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PI4KII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PI4KII BINDING SITE, designated SEQ ID:20481, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43702] Another function of VGAM1220 is therefore inhibition of PI4KII (Accession NM_018425). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PI4KII. Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215) is another VGAM1220 host target gene. TGOLN2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TGOLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGOLN2 BINDING SITE, designated SEQ ID:32025, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43703] Another function of VGAM1220 is therefore inhibition of Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGOLN2. LOC126353 (Accession XM_059034) is another VGAM1220 host target gene. LOC126353 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC126353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC126353 BINDING SITE, designated SEQ ID:36828, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43704] Another function of VGAM1220 is therefore inhibition of LOC126353 (Accession XM_059034). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126353. LOC151475 (Accession XM_098063) is another VGAM1220 host target gene. LOC151475 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151475 BINDING SITE, designated SEQ ID:41353, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43705] Another function of VGAM1220 is therefore inhibition of LOC151475 (Accession XM_098063). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151475. LOC197423 (Accession XM_085436) is an-

other VGAM1220 host target gene. LOC197423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197423 BINDING SITE, designated SEQ ID:38143, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43706] Another function of VGAM1220 is therefore inhibition of LOC197423 (Accession XM_085436). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197423. LOC200138 (Accession XM_117194) is another VGAM1220 host target gene. LOC200138 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200138 BINDING SITE, designated SEQ ID:43279, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43707] Another function of VGAM1220 is therefore inhibition of LOC200138 (Accession XM_117194). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200138. LOC220753 (Accession XM_167549) is another VGAM1220 host target gene. LOC220753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220753 BINDING SITE, designated SEQ ID:44663, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43708] Another function of VGAM1220 is therefore inhibition of LOC220753 (Accession XM_167549). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220753. LOC254559 (Accession XM_172931) is another VGAM1220 host target gene. LOC254559 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254559, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254559 BINDING SITE, designated SEQ ID:46195, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43709] Another function of VGAM1220 is therefore inhibition of LOC254559 (Accession XM_172931). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254559. LOC57795 (Accession XM_045110) is another VGAM1220 host target gene. LOC57795 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC57795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57795 BINDING SITE, designated SEQ ID:34358, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43710] Another function of VGAM1220 is therefore inhibition of LOC57795 (Accession XM_045110). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC57795. LOC90120 (Accession XM_029168) is another VGAM1220 host target gene. LOC90120 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90120 BINDING SITE, designated SEQ ID:30853, to the nucleotide sequence of VGAM1220 RNA, herein designated VGAM RNA, also designated SEQ ID:3931.

[43711] Another function of VGAM1220 is therefore inhibition of LOC90120 (Accession XM_029168). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90120. LOC93613 (Accession XM_052568) is another VGAM1220 host target gene. LOC93613 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93613, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93613 BINDING SITE, designated SEQ ID:35994, to the nucleotide sequence of VGAM1220 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3931.

[43712] Another function of VGAM1220 is therefore inhibition of LOC93613 (Accession XM_052568). Accordingly, utilities of VGAM1220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93613. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1221 (VGAM1221) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43713] VGAM1221 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1221 was detected is described hereinabove with reference to Figs. 1–8.

[43714] VGAM1221 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43715] VGAM1221 gene encodes a VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1221 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1221 precursor RNA is designated SEQ ID:1207, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1207 is located at position 26938 relative to the genome of Fowl Adenovirus D.

- [43716] VGAM1221 precursor RNA folds onto itself, forming VGAM1221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [43717] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1221 folded precursor RNA into VGAM1221 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1221 RNA is designated SEQ ID:3932, and is provided hereinbelow with reference to the sequence listing part.

[43718] VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1221 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43719] VGAM1221 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1221 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1221 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43720] The complementary binding of VGAM1221 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1221 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1221 host target RNA into VGAM1221 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43721] It is appreciated that VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1221 host target genes. The mRNA of

each one of this plurality of VGAM1221 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1221 RNA, herein designated VGAM RNA, and which when bound by VGAM1221 RNA causes inhibition of translation of respective one or more VGAM1221 host target proteins.

[43722] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1221 gene, herein designated VGAM GENE, on one or more VGAM1221 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[43723] It is yet further appreciated that a function of VGAM1221 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1221 correlate with, and may be deduced from, the identity of the host target genes which VGAM1221 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43724] Nucleotide sequences of the VGAM1221 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1221 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1221 are further described hereinbelow with reference to Table 1.

[43725] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1221 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1221 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43726] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1221 gene, herein designated VGAM is inhibition of expression of VGAM1221 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1221 correlate with, and may be deduced from, the identity of the target genes which VGAM1221 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43727] Diptheria Toxin Resistance Protein Required For Dipthamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Accession NM_001384) is a VGAM1221 host target gene. DPH2L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPH2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPH2L2 BINDING SITE, designated SEQ ID:7059, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43728] A function of VGAM1221 is therefore inhibition of Dipthe-

ria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Accession NM_001384), a gene which is required for diphthamide biosynthesis. Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPH2L2. The function of DPH2L2 has been established by previous studies. Diphtheria toxin inhibits eukaryotic protein synthesis by ADP-ribosylating diphthamide, a posttranslationally modified histidine residue present in EF2 (OMIM Ref. No. 130610)(Foley et al., 1995). Mattheakis et al. (1993) found that *dph2*, a *S. cerevisiae* diphtheria resistance gene, encodes a protein involved in diphthamide biosynthesis. By searching an EST database, Schultz et al. (1998) identified a human cDNA with 63% identity to the corresponding nucleotide sequence of human DPH2-like 1 (DPH2L1/OVCA1; 603527). Using a PCR strategy, they recovered cDNAs corresponding to the entire coding region of the gene, which they called DPH2L2. The predicted 489-amino acid protein shared 24% and 28% sequence identity with DPH2L1 and yeast *dph2*, respectively. Northern blot analysis revealed that DPH2L2 was expressed ubiquitously as a 2.5-kb mRNA. An additional 3-kb tran-

script was found in several tissues. By fluorescence in situ hybridization, Schultz et al. (1998) mapped the DPH2L2 gene to 1p34.

[43729] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43730] Foley, B. T.; Moehring, J. M.; Moehring, T. J. : Mutations in the elongation factor 2 gene which confer resistance to diphtheria toxin and Pseudomonas exotoxin A: genetic and biochemical analyses. J. Biol. Chem. 270: 23218–23225, 1995. ; and

[43731] Schultz, D. C.; Balasara, B. R.; Testa, J. R.; Godwin, A. K. : Cloning and localization of a human diphthamide biosynthesis-like protein-2 gene, DPH2L2. Genomics 52: 186–191, 1998.

[43732] Further studies establishing the function and utilities of DPH2L2 are found in John Hopkins OMIM database record ID 603456, and in cited publications numbered 5983–5985 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395) is another VGAM1221 host target gene. DYRK1A BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28166, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43733] Another function of VGAM1221 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Interleukin 2 Receptor, Beta (IL2RB, Accession NM_000878) is another VGAM1221 host target gene. IL2RB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL2RB, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL2RB BINDING SITE, designated SEQ ID:6568, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43734] Another function of VGAM1221 is therefore inhibition of Interleukin 2 Receptor, Beta (IL2RB, Accession NM_000878), a gene which is involved in receptor mediated endocytosis and transduces the mitogenic signals of il-2. Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL2RB. The function of IL2RB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM450. Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896) is another VGAM1221 host target gene. VPS26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS26 BINDING SITE, designated SEQ ID:11324, to the nucleotide se-

quence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43735] Another function of VGAM1221 is therefore inhibition of Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896), a gene which is a sorting protein– ensures the proper delivery of organelle–specific proteins. Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS26. The function of VPS26 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM315. Cystatin F (leukocystatin) (CST7, Accession NM_003650) is another VGAM1221 host target gene. CST7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CST7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CST7 BINDING SITE, designated SEQ ID:9725, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43736] Another function of VGAM1221 is therefore inhibition of

Cystatin F (leukocystatin) (CST7, Accession NM_003650). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CST7. Forkhead Box D4 (FOXD4, Accession XM_095746) is another VGAM1221 host target gene. FOXD4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOXD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXD4 BINDING SITE, designated SEQ ID:40281, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43737] Another function of VGAM1221 is therefore inhibition of Forkhead Box D4 (FOXD4, Accession XM_095746). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXD4. KIAA0427 (Accession NM_014772) is another VGAM1221 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16570, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43738] Another function of VGAM1221 is therefore inhibition of KIAA0427 (Accession NM_014772). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. KIAA0794 (Accession XM_087353) is another VGAM1221 host target gene. KIAA0794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0794 BINDING SITE, designated SEQ ID:39182, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43739] Another function of VGAM1221 is therefore inhibition of KIAA0794 (Accession XM_087353). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0794. KIAA0820 (Accession XM_044463) is another VGAM1221 host target gene. KIAA0820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0820 BINDING SITE, designated SEQ ID:34216, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43740] Another function of VGAM1221 is therefore inhibition of KIAA0820 (Accession XM_044463). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0820. KIAA1024 (Accession XM_044580) is another VGAM1221 host target gene. KIAA1024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1024 BINDING SITE, designated SEQ ID:34233, to the

nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43741] Another function of VGAM1221 is therefore inhibition of KIAA1024 (Accession XM_044580). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1024. KIAA1265 (Accession XM_047707) is another VGAM1221 host target gene. KIAA1265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1265 BINDING SITE, designated SEQ ID:35030, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43742] Another function of VGAM1221 is therefore inhibition of KIAA1265 (Accession XM_047707). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1265. MGC2487 (Accession NM_023932) is another VGAM1221 host target gene. MGC2487 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by MGC2487, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2487 BINDING SITE, designated SEQ ID:23422, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43743] Another function of VGAM1221 is therefore inhibition of MGC2487 (Accession NM_023932). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2487. Mitochondrial Ribosomal Protein S11 (MRPS11, Accession NM_022839) is another VGAM1221 host target gene. MRPS11 BINDING SITE1 and MRPS11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MRPS11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS11 BINDING SITE1 and MRPS11 BINDING SITE2, designated SEQ ID:23126 and SEQ ID:45376 respectively, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43744] Another function of VGAM1221 is therefore inhibition of Mitochondrial Ribosomal Protein S11 (MRPS11, Accession NM_022839). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS11. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_020550) is another VGAM1221 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING SITE4, designated SEQ ID:21758, SEQ ID:21766, SEQ ID:14841 and SEQ ID:15764 respectively, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43745] Another function of VGAM1221 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_020550). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. LOC152674 (Accession XM_098251) is another VGAM1221 host target

gene. LOC152674 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152674 BINDING SITE, designated SEQ ID:41537, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43746] Another function of VGAM1221 is therefore inhibition of LOC152674 (Accession XM_098251). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152674. LOC163782 (Accession XM_089138) is another VGAM1221 host target gene. LOC163782 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC163782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163782 BINDING SITE, designated SEQ ID:39966, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43747] Another function of VGAM1221 is therefore inhibition of LOC163782 (Accession XM_089138). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163782. LOC56965 (Accession NM_020214) is another VGAM1221 host target gene. LOC56965 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56965 BINDING SITE, designated SEQ ID:21456, to the nucleotide sequence of VGAM1221 RNA, herein designated VGAM RNA, also designated SEQ ID:3932.

[43748] Another function of VGAM1221 is therefore inhibition of LOC56965 (Accession NM_020214). Accordingly, utilities of VGAM1221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56965. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1222 (VGAM1222) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[43749] VGAM1222 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1222 was detected is described hereinabove with reference to Figs. 1-8.

[43750] VGAM1222 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowl Adenovirus D. VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43751] VGAM1222 gene encodes a VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1222 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1222 precursor RNA is designated SEQ ID:1208, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1208 is located at position 25411 relative to the genome of Fowl Adenovirus D.

[43752] VGAM1222 precursor RNA folds onto itself, forming VGAM1222 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43753] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1222 folded precursor RNA into VGAM1222 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1222 RNA is designated SEQ ID:3933, and is provided hereinbelow with reference to the sequence listing part.

[43754] VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1222 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43755] VGAM1222 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1222 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1222 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43756] The complementary binding of VGAM1222 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1222 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1222 host target RNA into VGAM1222 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43757] It is appreciated that VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1222 host target genes. The mRNA of each one of this plurality of VGAM1222 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1222 RNA, herein designated VGAM RNA, and which when bound by VGAM1222 RNA causes inhibition of translation of respective one or more VGAM1222 host target proteins.

[43758] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1222 gene, herein designated VGAM GENE, on one or more VGAM1222 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43759] It is yet further appreciated that a function of VGAM1222 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1222 include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGAM1222 correlate with, and may be deduced from, the identity of the host target genes which VGAM1222 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[43760] Nucleotide sequences of the VGAM1222 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1222 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1222 are further described hereinbelow with reference to Table 1.

[43761] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1222 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1222 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43762] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1222 gene, herein designated VGAM is inhibition of expression of VGAM1222 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1222 correlate with, and may be deduced from, the identity of the target genes which VGAM1222 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43763] RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM_002879) is a VGAM1222 host target gene. RAD52 BINDING SITE1 through RAD52 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD52, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE1 through RAD52 BINDING SITE4, designated SEQ ID:8790, SEQ ID:28647, SEQ ID:28655 and SEQ ID:28664 respectively, to the nucleotide sequence of VGAM1222 RNA, herein designated VGAM RNA, also designated SEQ ID:3933.

[43764] A function of VGAM1222 is therefore inhibition of RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM_002879). Accordingly, utilities of VGAM1222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. KIAA0286 (Accession XM_043118) is another VGAM1222 host target gene. KIAA0286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0286 BINDING SITE, designated SEQ ID:33907, to the nucleotide sequence of VGAM1222 RNA, herein designated VGAM RNA, also designated SEQ ID:3933.

[43765] Another function of VGAM1222 is therefore inhibition of KIAA0286 (Accession XM_043118). Accordingly, utilities of VGAM1222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0286. Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211) is another VGAM1222 host target gene. LOXL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOXL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL4 BINDING SITE, designated SEQ ID:25929, to the nucleotide sequence of VGAM1222 RNA, herein designated VGAM RNA, also designated SEQ ID:3933.

[43766] Another function of VGAM1222 is therefore inhibition of Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211). Accordingly, utilities of VGAM1222 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with LOXL4. LOC201696 (Accession XM_032269) is another VGAM1222 host target gene. LOC201696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201696 BINDING SITE, designated SEQ ID:31622, to the nucleotide sequence of VGAM1222 RNA, herein designated VGAM RNA, also designated SEQ ID:3933.

[43767] Another function of VGAM1222 is therefore inhibition of LOC201696 (Accession XM_032269). Accordingly, utilities of VGAM1222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1223 (VGAM1223) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43768] VGAM1223 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1223 was detected is described hereinabove with reference to Figs. 1–8.

[43769] VGAM1223 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43770] VGAM1223 gene encodes a VGAM1223 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1223 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1223 precursor RNA is designated SEQ ID:1209, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1209 is located at position 143093 relative to the genome of Equine Herpesvirus 2.

[43771] VGAM1223 precursor RNA folds onto itself, forming VGAM1223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43772] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1223 folded precursor RNA into VGAM1223 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1223 RNA is designated SEQ ID:3934, and is provided hereinbelow with reference to the sequence listing part.

[43773] VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1223 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[43774] VGAM1223 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1223 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1223 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43775] The complementary binding of VGAM1223 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1223 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1223 host target RNA into VGAM1223 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43776] It is appreciated that VGAM1223 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1223 host target genes. The mRNA of each one of this plurality of VGAM1223 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1223 RNA, herein designated VGAM RNA, and which when bound by VGAM1223 RNA causes inhibition of translation of respective one or more VGAM1223 host target proteins.

[43777] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1223 gene, herein designated VGAM GENE, on one or more VGAM1223 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43778] It is yet further appreciated that a function of VGAM1223 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1223 correlate with, and may be deduced from, the identity of the host target genes which VGAM1223 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43779] Nucleotide sequences of the VGAM1223 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1223 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1223 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1223 are further
described hereinbelow with reference to Table 1.

[43780] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1223 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1223 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[43781] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1223 gene, herein designated VGAM is
inhibition of expression of VGAM1223 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1223 correlate with, and may be deduced
from, the identity of the target genes which VGAM1223
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[43782] UDP-GlcNAc:betaGal Beta-
1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Acces-

sion NM_014256) is a VGAM1223 host target gene.

B3GNT3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B3GNT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT3 BINDING SITE, designated SEQ ID:15531, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43783] A function of VGAM1223 is therefore inhibition of UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Accession NM_014256). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT3. CERD4 (Accession NM_012074) is another VGAM1223 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14348, to the nucleotide sequence of

VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43784] Another function of VGAM1223 is therefore inhibition of CERD4 (Accession NM_012074). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. Cryptochrome 2 (photolyase-like) (CRY2, Accession XM_051030) is another VGAM1223 host target gene. CRY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRY2 BINDING SITE, designated SEQ ID:35730, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43785] Another function of VGAM1223 is therefore inhibition of Cryptochrome 2 (photolyase-like) (CRY2, Accession XM_051030), a gene which has a role in circadian photoreception in mammals. Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRY2. The function of CRY2 has been established by previous

studies. Hsu et al. (1996) identified a human gene, CRY2, whose product had 73% amino acid identity to the human (6-4)photolyase (CRY1; 601933). The CRY2 protein shares 51% amino acid sequence identity to *Drosophila* (6-4)photolyase. Hsu et al. (1996) purified the human CRY1 and CRY2 proteins and characterized them as maltose-binding fusion proteins that contain FAD and a pterin cofactor. Both CRY1 and CRY2 proteins lacked photolyase activity. Hsu et al. (1996) concluded that these proteins are not photolyases, but may function as blue-light photoreceptors in humans. As part of a search for human brain cDNA clones with the potential to encode large proteins in vitro, Ishikawa et al. (1998) independently identified CRY2. The CRY2 open reading frame encodes a protein of 589 amino acids with an apparent molecular mass of 67 kD. Animal model experiments lend further support to the function of CRY2. Yagita et al. (2001) used wildtype and *Cry1* $-/-$ and *Cry2* $-/-$ deficient cell lines derived from *Cry* mutant mice to demonstrate that the peripheral oscillator in cultured fibroblasts is identical to the oscillator in the suprachiasmatic nucleus in (1) temporal expression profiles of all known clock genes; (2) the phase of the various mRNA rhythms (i.e.,

antiphase oscillation of Bmal1 (OMIM Ref. No. 602550) and Per); (3) the delay between maximum mRNA levels and appearance of nuclear Per1 and Per2 protein; (4) the inability to produce oscillations in the absence of functional Cry genes; and (5) the control of period length by Cry proteins

[43786] It is appreciated that the abovementioned animal model for CRY2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[43787] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43788] Hsu, D. S.; Zhao, X.; Zhao, S.; Kazantsev, A.; Wang, R.-P.; Todo, T.; Wei, Y.-F.; Sancar, A. : Putative human blue-light photoreceptors hCRY1 and hCRY2 are flavoproteins. Biochemistry 35: 13871–13877, 1996. ; and

[43789] Yagita, K.; Tamanini, F.; van der Horst, G. T. J.; Okamura, H. : Molecular mechanisms of the biological clock in cultured fibroblasts. Science 292: 278–281, 2001.

[43790] Further studies establishing the function and utilities of CRY2 are found in John Hopkins OMIM database record ID 603732, and in cited publications numbered 6258–6260,

9440–6264, 1256, 584 and 6266–6267 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nucleoporin 98kDa (NUP98, Accession NM_016320) is another VGAM1223 host target gene. NUP98 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP98 BINDING SITE, designated SEQ ID:18439, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43791] Another function of VGAM1223 is therefore inhibition of Nucleoporin 98kDa (NUP98, Accession NM_016320), a gene which functions in the nuclear transport of protein and RNA. Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP98. The function of NUP98 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Chromosome 20 Open Reading Frame 103

(C20orf103, Accession NM_012261) is another VGAM1223 host target gene. C20orf103 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf103 BINDING SITE, designated SEQ ID:14568, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43792] Another function of VGAM1223 is therefore inhibition of Chromosome 20 Open Reading Frame 103 (C20orf103, Accession NM_012261). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf103. CAMP-GEFII (Accession NM_007023) is another VGAM1223 host target gene. CAMP-GEFII BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMP-GEFII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMP-GEFII BINDING SITE, designated SEQ ID:13879, to

the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43793] Another function of VGAM1223 is therefore inhibition of CAMP-GEFII (Accession NM_007023). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMP-GEFII. Fidgetin (FIGN, Accession XM_171005) is another VGAM1223 host target gene. FIGN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FIGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FIGN BINDING SITE, designated SEQ ID:45775, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43794] Another function of VGAM1223 is therefore inhibition of Fidgetin (FIGN, Accession XM_171005). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FIGN. FLJ10044 (Accession NM_017980) is another VGAM1223 host target gene. FLJ10044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ10044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10044 BINDING SITE, designated SEQ ID:19709, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43795] Another function of VGAM1223 is therefore inhibition of FLJ10044 (Accession NM_017980). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10044. FLJ22283 (Accession NM_032220) is another VGAM1223 host target gene. FLJ22283 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22283 BINDING SITE, designated SEQ ID:25946, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43796] Another function of VGAM1223 is therefore inhibition of FLJ22283 (Accession NM_032220). Accordingly, utilities of

VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22283. KIAA0939 (Accession XM_030524) is another VGAM1223 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31056, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43797] Another function of VGAM1223 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA1111 (Accession XM_171233) is another VGAM1223 host target gene. KIAA1111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1111 BINDING SITE, designated SEQ ID:46017, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43798] Another function of VGAM1223 is therefore inhibition of KIAA1111 (Accession XM_171233). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1111. Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM_130843) is another VGAM1223 host target gene. PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2, designated SEQ ID:28373 and SEQ ID:28368 respectively, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43799] Another function of VGAM1223 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM_130843). Accordingly, util-

ities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRN2. LOC146880 (Accession XM_085627) is another VGAM1223 host target gene. LOC146880 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146880, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146880 BINDING SITE, designated SEQ ID:38256, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43800] Another function of VGAM1223 is therefore inhibition of LOC146880 (Accession XM_085627). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146880. LOC151507 (Accession XM_087225) is another VGAM1223 host target gene. LOC151507 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC151507 BINDING SITE, designated SEQ ID:39125, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43801] Another function of VGAM1223 is therefore inhibition of LOC151507 (Accession XM_087225). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151507. LOC168576 (Accession XM_095191) is another VGAM1223 host target gene. LOC168576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168576 BINDING SITE, designated SEQ ID:40254, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43802] Another function of VGAM1223 is therefore inhibition of LOC168576 (Accession XM_095191). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168576. LOC196955 (Accession XM_085210) is another VGAM1223 host target gene. LOC196955 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37935, to the nucleotide sequence of VGAM1223 RNA, herein designated VGAM RNA, also designated SEQ ID:3934.

[43803] Another function of VGAM1223 is therefore inhibition of LOC196955 (Accession XM_085210). Accordingly, utilities of VGAM1223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1224 (VGAM1224) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43804] VGAM1224 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1224 was detected is described hereinabove with reference to Figs. 1-8.

[43805] VGAM1224 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43806] VGAM1224 gene encodes a VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1224 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1224 precursor RNA is designated SEQ ID:1210, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1210 is located at position 141418 relative to the genome of Equine Herpesvirus 2.

[43807] VGAM1224 precursor RNA folds onto itself, forming VGAM1224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[43808] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1224 folded precursor RNA into VGAM1224 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1224 RNA is designated SEQ ID:3935, and is provided hereinbelow with reference to the sequence listing part.

[43809] VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1224 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43810] VGAM1224 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1224 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1224 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1224 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43811] The complementary binding of VGAM1224 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1224 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1224 host target RNA into VGAM1224 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43812] It is appreciated that VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1224 host target genes. The mRNA of each one of this plurality of VGAM1224 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1224 RNA, herein designated VGAM RNA, and which when bound by VGAM1224 RNA causes inhibition of translation of respective one or more VGAM1224 host target proteins.

[43813] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1224 gene, herein designated VGAM GENE, on one or more VGAM1224 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43814] It is yet further appreciated that a function of VGAM1224 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1224 correlate with, and may be deduced from, the identity of the host target genes which VGAM1224 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43815] Nucleotide sequences of the VGAM1224 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1224 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1224 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1224 are further described hereinbelow with reference to Table 1.

[43816] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1224 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1224 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43817] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1224 gene, herein designated VGAM is inhibition of expression of VGAM1224 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1224 correlate with, and may be deduced from, the identity of the target genes which VGAM1224 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43818] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974) is a VGAM1224 host target gene. AKAP13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:43181, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43819] A function of VGAM1224 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17. BCL2-like 2 (BCL2L2, Accession NM_004050) is another VGAM1224 host target gene. BCL2L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L2 BINDING SITE, designated SEQ ID:10260, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ

ID:3935.

[43820] Another function of VGAM1224 is therefore inhibition of BCL2-like 2 (BCL2L2, Accession NM_004050), a gene which promotes cell survival. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L2. The function of BCL2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM431.CD244 (Accession NM_016382) is another VGAM1224 host target gene. CD244 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD244 BINDING SITE, designated SEQ ID:18525, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43821] Another function of VGAM1224 is therefore inhibition of CD244 (Accession NM_016382), a gene which can interfere with a step as proximal as phosphorylation of an activation receptor. Accordingly, utilities of VGAM1224 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with CD244. The function of CD244 has been established by previous studies. By screening a genomic DNA library and probing with mouse 2b4, followed by screening a human NK-cell cDNA library, Boles et al. (1999) isolated a cDNA encoding human 2B4. Sequence analysis predicted that the 365-amino acid protein, which is 70% similar to the mouse sequence and approximately 45% similar to other members of the CD2 family, has an 18-amino acid leader sequence; an extracellular region of 204 amino acids with 2 Ig-like motifs and 8 potential N-linked glycosylation sites; a 24-amino acid transmembrane domain; and a 120-amino acid cytoplasmic tail with 6 tyrosine residues. Northern blot analysis detected 3- and 5-kb transcripts in T- and NK-cell lines; however, peripheral blood leukocytes, spleen, and lymph node expressed only the 3-kb transcript. Southern blot analysis determined that the 2B4 gene spans approximately 25 kb. Functional analysis demonstrated that engagement of 2B4 with specific antibody activates NK cytolytic activity. By studying NK-cell function in patients with X-linked lymphoproliferative disease (XLPD; 308240) and a defect in the SAP gene, Parolini et al. (2000) found

that a number of triggering receptors displayed normal function. However, upon 2B4 interaction with CD48, NK-cell function against Epstein Barr virus (EBV)-infected cells, which is primarily mediated via NKp46 (LY94; 604530), was inhibited. Disruption of 2B4-CD48 and/or NK receptor-HLA interaction restored NK cytolytic activity. RT-PCR analysis detected the full-length 2B4 cDNA as well as a 2B4 molecule lacking the Ig C2 domain in both patients and normal individuals. Molecular analysis failed to reveal any differences between normal and patient 2B4 sequences. Immunoblot analysis showed that treatment of normal but not XLPD NK cells with pervanadate led to the association of 2B4 with SAP. Parolini et al. (2000) suggested that anti-2B4 treatment might be of use in XLPD patients awaiting bone marrow transplantation.

[43822] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43823] Parolini, S.; Bottino, C.; Falco, M.; Augugliaro, R.; Giliani, S.; Franceschini, R.; Ochs, H. D.; Wolf, H.; Bonnefoy, J.-Y.; Biassoni, R.; Moretta, L.; Notarangelo, L. D.; Moretta, A. : X-linked lymphoproliferative disease: 2B4 molecules displaying inhibitory rather than activating function are re-

sponsible for the inability of natural killer cells to kill Epstein-Barr virus-infected cells. J. Exp. Med. 192: 337-346, 2000. ; and

[43824] Boles, K. S.; Nakajima, H.; Colonna, M.; Chuang, S. S.; Stepp, S. E.; Bennett, M.; Kumar, V.; Mathew, P. A. : Molecular characterization of a novel human natural killer cell receptor ho.

[43825] Further studies establishing the function and utilities of CD244 are found in John Hopkins OMIM database record ID 605554, and in cited publications numbered 8597, 972, 4213, 877 and 973 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDC5 Cell Division Cycle 5-like (*S. pombe*) (CDC5L, Accession NM_001253) is another VGAM1224 host target gene. CDC5L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDC5L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC5L BINDING SITE, designated SEQ ID:6923, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43826] Another function of VGAM1224 is therefore inhibition of CDC5 Cell Division Cycle 5-like (*S. pombe*) (CDC5L, Accession NM_001253). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC5L. Dachshund Homolog (*Drosophila*) (DACH, Accession NM_080759) is another VGAM1224 host target gene. DACH BINDING SITE1 and DACH BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DACH, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DACH BINDING SITE1 and DACH BINDING SITE2, designated SEQ ID:28037 and SEQ ID:28041 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43827] Another function of VGAM1224 is therefore inhibition of Dachshund Homolog (*Drosophila*) (DACH, Accession NM_080759), a gene which regulates early progenitor cell proliferation during retinogenesis and pituitary development. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with DACH. The function of DACH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM260. Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM_001418) is another VGAM1224 host target gene. EIF4G2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EIF4G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4G2 BINDING SITE, designated SEQ ID:7116, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43828] Another function of VGAM1224 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 2 (EIF4G2, Accession NM_001418), a gene which is a repressor of translation. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4G2. The function of EIF4G2 and its association with various diseases and clinical conditions, has been established by previous

studies, as described hereinabove with reference to VGAM1065. Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM_130442) is another VGAM1224 host target gene. ELMO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELMO1 BINDING SITE, designated SEQ ID:28205, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43829] Another function of VGAM1224 is therefore inhibition of Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM_130442). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELMO1. FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801) is another VGAM1224 host target gene. FKBP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKBP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FKBP1A BINDING SITE, designated SEQ ID:6476, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43830] Another function of VGAM1224 is therefore inhibition of FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801), a gene which FK506-binding protein 1A. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP1A. The function of FKBP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57.GDNF Family Receptor Alpha 2 (GFRA2, Accession NM_001495) is another VGAM1224 host target gene. GFRA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFRA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFRA2 BINDING SITE, designated SEQ ID:7242, to the nucleotide sequence of VGAM1224 RNA, herein designated

VGAM RNA, also designated SEQ ID:3935.

[43831] Another function of VGAM1224 is therefore inhibition of GDNF Family Receptor Alpha 2 (GFRA2, Accession NM_001495), a gene which mediates the nrtn-induced autophosphorylation and activation of the ret receptor. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFRA2. The function of GFRA2 has been established by previous studies. Glial cell line-derived neurotrophic factor (GDNF; 600837) is a potent survival factor for central dopaminergic neurons, motor neurons, and several other populations of neurons in the central and peripheral nervous systems. The GDNF signal is mediated by a complex of the receptor tyrosine kinase RET (OMIM Ref. No. 164761) and a glycosylphosphatidylinositol (GPI)-linked protein, GDNF receptor-alpha (GDNFRA; 601496). Suvanto et al. (1997) cloned the human and rat cDNA sequences of GDNFR-beta, a gene encoding a 464-amino acid homolog of GDNFR-alpha. By fluorescence in situ hybridization, they assigned the GDNFRB gene to 8p22-p21. In addition, the mouse Gdnfrb gene was assigned to 14D3-E1. Similarly to GDNFR-alpha, GDNFR-beta mediates GDNF-induced RET autophospho-

rylation in transfected cells. By Northern hybridization, Suvanto et al. (1997) showed that the transcript level of human GDNFR-beta mRNA is high in the adult brain, intestine, and placenta, and in fetal brain, lung, and kidney. By in situ hybridization, they demonstrated that GDNFRB mRNA shows in the rat embryo a different distribution to that of GDNFRA mRNA, especially in adrenal gland, kidney, and gut. In the developing nervous system, GDNFRB mRNA expression was restricted to certain neuronal populations, while GDNFRA mRNA was widely expressed also in nonneuronal cells. Distinct tissue distribution of GDNFRB mRNA and its ability to mediate GDNF signal in transfected cells suggested a role in signal transduction of GDNF and, possibly, related neurotrophic factors in vivo. Baloh et al. (1997) independently described the cloning and initial characterization of a second coreceptor for both neurturin (NRTN; 602018) and GDNF signaling. To name the receptors appropriately for their ability to function in both GDNF and NRTN signaling, the authors referred to them as TGF-beta-related neurotrophic factor receptors 1 and 2 (TrnR1 and TmR2), where TmR1 corresponds to GDNFR-alpha. By fluorescence in situ hybridization, they mapped the gene to 8p21-p12; 8p21 is a

consensus assignment. See also the reports by Klein et al. (1997) and Sanicola et al. (1997). Various nomenclature systems have been used to describe this gene.

[43832] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43833] Baloh, R. H.; Tansey, M. G.; Golden, J. P.; Creedon, D. J.; Heuckeroth, R. O.; Keck, C. L.; Zimonjic, D. B.; Popescu, N. C.; Johnson, E. M., Jr.; Milbrandt, J. : TrnR2, a novel receptor that mediates neurturin and GDNF signaling through Ret. Neuron 18: 793–802, 1997. ; and

[43834] Klein, R. D.; Sherman, D.; Ho, W.-H.; Stone, D.; Bennett, G. L.; Moffat, B.; Vandlen, R.; Simmons, L.; Gu, Q.; Hongo, J.-A.; Devaux, B.; Poulsen, K.; Armanini, M.; Nozaki, C.; Asai, N.;

[43835] Further studies establishing the function and utilities of GFRA2 are found in John Hopkins OMIM database record ID 601956, and in cited publications numbered 634 and 5816–5818 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843) is another VGAM1224 host target gene. GRM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM6 BINDING SITE, designated SEQ ID:6510, to the nucleotide sequence of VGAM1224 RNA, herein

designated VGAM RNA, also designated SEQ ID:3935.

[43836] Another function of VGAM1224 is therefore inhibition of Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM6. Immunoglobulin Mu Binding Protein 2 (IGHMBP2, Accession NM_002180) is another VGAM1224 host target gene. IGHMBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGHMBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGHMBP2 BINDING SITE, designated SEQ ID:7938, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43837] Another function of VGAM1224 is therefore inhibition of Immunoglobulin Mu Binding Protein 2 (IGHMBP2, Accession NM_002180). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGHMBP2. LFG (Accession XM_084780) is another VGAM1224 host target gene. LFG BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LFG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFG BINDING SITE, designated SEQ ID:37697, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43838] Another function of VGAM1224 is therefore inhibition of LFG (Accession XM_084780). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFG. LIM Domain Only 1 (rhombotin 1) (LMO1, Accession NM_002315) is another VGAM1224 host target gene. LMO1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO1 BINDING SITE, designated SEQ ID:8129, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43839] Another function of VGAM1224 is therefore inhibition of LIM Domain Only 1 (rhombotin 1) (LMO1, Accession

NM_002315). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO1. Phosphogluconate Dehydrogenase (PGD, Accession XM_086151) is another VGAM1224 host target gene. PGD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PGD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGD BINDING SITE, designated SEQ ID:38524, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43840] Another function of VGAM1224 is therefore inhibition of Phosphogluconate Dehydrogenase (PGD, Accession XM_086151), a gene which catalyzes a step in the pentose phosphate pathway, oxidates glucose-6-phosphate into 6-phosphoglucono-lactone. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGD. The function of PGD has been established by previous studies. Brewer and Dern (1964) reported deficiency of 6-phosphogluconate dehydrogenase (6PGD), the second

dehydrogenase in the pentose phosphate shunt, in 10 members of 4 generations of an American black family. They concluded that the inheritance is autosomal dominant, all 6PGD-deficient persons observed being heterozygotes. However, no male-to-male transmission was observed; indeed, no offspring of affected males were tested. Against X-linkage is the fact that the average enzyme level in 3 6PGD-deficient males was somewhat higher than that in seven 6PGD-deficient females. The opposite would be expected of an X-linked trait. The authors commented on the autosomal control of an enzyme that is closely related metabolically to G6PD, an enzyme determined by an X-linked gene. In a survey of unrelated persons, Dern et al. (1966) found in 3 of 873 American blacks and 2 of 275 Caucasians a reduction in erythrocyte 6-phosphogluconate dehydrogenase to the range of 42 to 65% of normal. Leukocyte enzyme was also reduced. No correlation was found between electrophoretic phenotype and the quantitative variation. The inheritance was clearly autosomal dominant. Using starch-gel electrophoresis, Fildes and Parr (1963) detected 2 distinct types of human red cell 6-phosphogluconate dehydrogenase. Ten of 150 random blood samples showed 2 broad, less distinct

bands in contrast to the single narrow, sharp band in the remainder. Inheritance appears to be autosomal, a point of particular note. Since the G6PD locus is X-linked, these 2 functionally related genes do not show clustering. Heterozygotes and homozygotes showed no quantitative difference in red blood cell 6PGD activity. Deficiency of this enzyme, with or without electrophoretic abnormality, has been observed (Parr, 1966). Nevo (1989) identified a rare PGD variant called PGD Mediterranean. Severe deficiency of 6PGD, although well-documented (Brewer and Dern, 1964; Dern et al., 1966; Parr and Fitch, 1967), has never been incriminated as the cause of hemolytic anemia. In fact, persons with less than 5% of normal activity in red cell enzymes, who were found in population surveys by Parr and Fitch (1967), were entirely asymptomatic. Beutler et al. (1985) found hemolysis in a subject in whom partial deficiency of 6PGD coexisted with G6PD deficiency, whereas no hemolysis was found in persons with the G6PD variant alone. A synergism of the 2 enzymopathies is possible

[43841] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43842] Beutler, E.; Kuhl, W.; Gelbart, T. :

6-Phosphogluconolactonase deficiency, a hereditary erythrocyte enzyme deficiency: possible interaction with glucose-6-phosphate dehydrogenase deficiency. Proc. Nat. Acad. Sci. 82: 3876-3878, 1985. ; and

[43843] Nevo, S. : A new rare PGD variant, PGD Mediterranean.

Hum. Genet. 81: 199 only, 1989.

[43844] Further studies establishing the function and utilities of

PGD are found in John Hopkins OMIM database record ID 172200, and in cited publications numbered 2104,

2105-2108, 557, 2109-2116, 346 and 3780-2122 listed

in the bibliography section hereinbelow, which are also

hereby incorporated by reference. Paired Mesoderm

Homeo Box 1 (PMX1, Accession NM_022716) is another

VGAM1224 host target gene. PMX1 BINDING SITE1 and

PMX1 BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by PMX1,

corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide se-

quences of PMX1 BINDING SITE1 and PMX1 BINDING SITE2,

designated SEQ ID:22918 and SEQ ID:13783 respectively,

to the nucleotide sequence of VGAM1224 RNA, herein

designated VGAM RNA, also designated SEQ ID:3935.

[43845] Another function of VGAM1224 is therefore inhibition of Paired Mesoderm Homeo Box 1 (PMX1, Accession NM_022716), a gene which acts as a transcriptional regulator of muscle creatine kinase. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMX1. The function of PMX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381. Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM_080591) is another VGAM1224 host target gene. PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTGS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2, designated SEQ ID:27899 and SEQ ID:12129 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43846] Another function of VGAM1224 is therefore inhibition of Prostaglandin–endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM_080591), a gene which may play an important role in regulating or promoting cell proliferation in some normal and neoplastically transformed cells. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS1. The function of PTGS1 has been established by previous studies. Prostaglandin H2 synthase is known to pharmacologists (Vane et al., 1994) as cyclooxygenase (COX), and its 2 isoforms are known as COX1 and COX2. Vane et al. (1994) outlined the actions of the 2 isoforms of COX. Stemming from this outline was a hypothesis that the therapeutic effects of drugs such as aspirin are due to inhibition of COX2, whereas the unwanted side-effects (and the action on platelets) result from inhibition of COX1. Prostaglandin–endoperoxide synthase (PTGS; EC 1.14.99.1; fatty acid cyclooxygenase; PGH synthase) is the key enzyme in prostaglandin biosynthesis. The cyclooxygenase activity of the enzyme is inhibited by nonsteroidal antiinflammatory drugs such as aspirin and endomethacin. Animal model experiments lend further sup-

port to the function of PTGS1. To study the separate roles of the 2 isoforms of cyclooxygenase, Langenbach et al. (1995) used homologous recombination to disrupt the mouse *Ptgs1* gene encoding COX1. Homozygous *Ptgs1* mutant mice survived well, had no gastric pathology, and showed less indomethacin-induced gastric ulceration than wildtype mice, even though their gastric prostaglandin E2 levels were about 1% of wildtype. Homozygous mutant mice had reduced platelet aggregation and a decreased inflammatory response to arachidonic acid, but not to tetradecanoyl phorbol acetate. *Ptgs1* homozygous mutant females mated to homozygous mutant males produced few live offspring. Langenbach et al. (1995) stated that COX1-deficient mice provided a useful model for distinguishing the physiologic roles of the 2 cyclooxygenases, COX1 and COX2.

[43847] It is appreciated that the abovementioned animal model for PTGS1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[43848] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [43849] Vane, J. R.; Mitchell, J. A.; Appleton, I.; Tomlinson, A.; Bishop-Bailey, D.; Croxtall, J.; Willoughby, D. A. : Inducible isoforms of cyclooxygenase and nitric-oxide synthase in inflammation. *Proc. Nat. Acad. Sci.* 91: 2046–2050, 1994. ; and
- [43850] Langenbach, R.; Morham, S. G.; Tiano, H. F.; Loftin, C. D.; Ghanayem, B. I.; Chulada, P. C.; Mahler, J. F.; Lee, C. A.; Goulding, E. H.; Kluckman, K. D.; Kim, H. S.; Smithies, O. : *Proc.*
- [43851] Further studies establishing the function and utilities of PTGS1 are found in John Hopkins OMIM database record ID 176805, and in cited publications numbered 10845–1085 and 10887–10889 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268) is another VGAM1224 host target gene. REQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by REQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REQ BINDING SITE, designated SEQ ID:12950, to the nucleotide sequence of VGAM1224

RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43852] Another function of VGAM1224 is therefore inhibition of Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268), a gene which is a putative zinc finger that is required for apoptosis in murine myeloid cell lines. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REQ. The function of REQ has been established by previous studies. Chestkov et al. (1996) described a conserved human gene homologous to neuro-d4 (OMIM Ref. No. 601670) which they designated ubi-d4. They mapped the gene to 11q13 by fluorescence in situ hybridization. The human protein is the apparent homolog of the mouse ubi-d4 or requiem protein (Gabig et al., 1994). Expression of ubi-d4/requiem appears to be required for apoptosis (Chestkov et al., 1996; Gabig et al., 1994). Apoptosis in murine myeloid cell lines requires the expression of the Requiem gene, which encodes a putative zinc finger protein. A large consortium (Gabig et al., 1998) consisting of 3 groups detected the protein in both cytoplasmic and nuclear subcellular fractions of murine myeloid cells and human K562 leukemia cells, which sug-

gested that the protein may have a function distinct from that of a transcription factor. The distribution did not alter upon apoptosis induction by IL3 deprivation. They showed, further, that the gene was expressed in various tissues in early gestational ages; however, expression was confined to testes, spleen, thymus, and part of the hippocampus in the adult mouse. The expression profile was considered consistent with a functional role during rapid growth and cell turnover, and again suggested a regulatory function for hematopoietic cells. The nucleotide sequence of the human cDNA was 73% identical overall to that of the murine cDNA. The human sequence encodes a 391-amino acid protein. By cohybridization fluorescence in situ hybridization on extended DNA fibers, the REQ gene was localized between MLK3 (OMIM Ref. No. 600050) and FAU (OMIM Ref. No. 134690), which had been mapped to 11q13, telomeric to PYGM (OMIM Ref. No. 232600). The physical distance between MLK3 and REQ was estimated to be 150 kb.

[43853] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43854] Gabig, T. G.; Mantel, P. L.; Rosli, R.; Crean, C. D. : Re-

quiem: a novel zinc finger gene essential for apoptosis in myeloid cells. J. Biol. Chem. 269: 29515–29519, 1994. ; and

[43855] Gabig, T. G.; Crean, C. D.; Klenk, A.; Long, H.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Quincey, D.; Parente, F.; Lespinasse, F.; Carle, G. F.; Gaudray, P.; and 13 others : Ex.

[43856] Further studies establishing the function and utilities of REQ are found in John Hopkins OMIM database record ID 601671, and in cited publications numbered 9402–9404 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAR–related Orphan Receptor B (RORB, Accession NM_006914) is another VGAM1224 host target gene. RORB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RORB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RORB BINDING SITE, designated SEQ ID:13787, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43857] Another function of VGAM1224 is therefore inhibition of

RAR-related Orphan Receptor B (RORB, Accession NM_006914), a gene which is an orphan nuclear receptor. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RORB. The function of RORB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM_001754) is another VGAM1224 host target gene. RUNX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RUNX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RUNX1 BINDING SITE, designated SEQ ID:7496, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43858] Another function of VGAM1224 is therefore inhibition of Runt-related Transcription Factor 1 (acute myeloid leukemia 1; aml1 oncogene) (RUNX1, Accession NM_001754). Accordingly, utilities of VGAM1224 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with RUNX1. Sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, fungal)-like (SC5DL, Accession XM_165583) is another VGAM1224 host target gene. SC5DL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SC5DL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SC5DL BINDING SITE, designated SEQ ID:43696, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43859] Another function of VGAM1224 is therefore inhibition of Sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, fungal)-like (SC5DL, Accession XM_165583). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SC5DL. Sialyltransferase 1 (beta-galactoside alpha-2,6-sialyltransferase) (SIAT1, Accession NM_003032) is another VGAM1224 host target gene. SIAT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SIAT1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT1 BINDING SITE, designated SEQ ID:8974, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43860] Another function of VGAM1224 is therefore inhibition of Sialyltransferase 1 (beta-galactoside alpha-2,6-sialyltransferase) (SIAT1, Accession NM_003032), a gene which transfers sialic acid from the donor of substrate cmp- sialic acid to galactose containing acceptor substrates. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT1. The function of SIAT1 has been established by previous studies. Much interest in the role and regulation of beta-galactoside alpha-2,6-sialyltransferase (EC 2.4.99.1) in B lymphocytes stemmed from its relation to CDw75, a human leukocyte cell-surface antigen expressed in mature and activated B cells but not in B cells at earlier stages of development or in plasma cells. SiaT-1 is required for the elaboration of the CDw75 cell-surface epitope. Grundmann et al. (1990) reported the complete cDNA sequence corresponding to

the SIAT1 gene on the basis of cDNA isolated from a human placental lambda-gt10 library. By Southern analysis of somatic cell hybrids and by in situ hybridization, Wang et al. (1993) demonstrated that the SIAT1 gene is located on 3q21-q28. Comparative analysis of the human and rat sequences demonstrated precise conservation of the intron/exon boundaries throughout the coding domains. Furthermore, there was extensive interspecies sequence similarity in some of the exons that contained information only for the 5-prime leader regions.

- [43861] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [43862] Grundmann, U.; Nerlich, C.; Rein, T.; Zettlmeissl, G. : Complete cDNA sequence encoding human beta-galactoside alpha-2,6-sialyltransferase. Nucleic Acids Res. 18: 667 only, 1990. ; and
- [43863] Wang, X.; Vertino, A.; Eddy, R. L.; Byers, M. G.; Jani-Sait, S. N.; Shows, T. B.; Lau, J. T. Y. : Chromosome mapping and organization of the human beta-galactoside alpha-2,6-sialyltrans.
- [43864] Further studies establishing the function and utilities of SIAT1 are found in John Hopkins OMIM database record ID

109675, and in cited publications numbered 3697–3698 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SRY (sex determining region Y)–box 4 (SOX4, Accession NM_003107) is another VGAM1224 host target gene. SOX4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX4 BINDING SITE, designated SEQ ID:9074, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43865] Another function of VGAM1224 is therefore inhibition of SRY (sex determining region Y)–box 4 (SOX4, Accession NM_003107), a gene which binds with high affinity to the t-cell enhancer motif 5'–aacaag–3' motif. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX4. The function of SOX4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM409. Transducin (beta)–like 1X–linked

(TBL1X, Accession NM_005647) is another VGAM1224 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BINDING SITE, designated SEQ ID:12181, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43866] Another function of VGAM1224 is therefore inhibition of Transducin (beta)-like 1X-linked (TBL1X, Accession NM_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. TIA1 Cytotoxic Granule-associated RNA Binding Protein-like 1 (TIAL1, Accession NM_022333) is another VGAM1224 host target gene. TIAL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

TIAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAL1 BINDING SITE, designated SEQ ID:22742, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43867] Another function of VGAM1224 is therefore inhibition of TIA1 Cytotoxic Granule-associated RNA Binding Protein-like 1 (TIAL1, Accession NM_022333), a gene which possesses nucleolytic activity against cytotoxic lymphocyte target cells. Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAL1. The function of TIAL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM350.Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723) is another VGAM1224 host target gene. ARHGEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ARHGEF2 BINDING SITE, designated SEQ ID:11090, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43868] Another function of VGAM1224 is therefore inhibition of Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF2. Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424) is another VGAM1224 host target gene. CECR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CECR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR1 BINDING SITE, designated SEQ ID:18885, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43869] Another function of VGAM1224 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 1 (CECR1, Accession NM_017424). Accordingly, utilities of

VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR1. DKFZp761K1824 (Accession NM_017597) is another VGAM1224 host target gene. DKFZp761K1824 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp761K1824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761K1824 BINDING SITE, designated SEQ ID:19059, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43870] Another function of VGAM1224 is therefore inhibition of DKFZp761K1824 (Accession NM_017597). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761K1824. Eukaryotic Translation Initiation Factor 4B (EIF4B, Accession XM_071605) is another VGAM1224 host target gene. EIF4B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EIF4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4B BINDING SITE, designated SEQ ID:37401, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43871] Another function of VGAM1224 is therefore inhibition of Eukaryotic Translation Initiation Factor 4B (EIF4B, Accession XM_071605). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4B. F-box Only Protein 21 (FBXO21, Accession NM_033624) is another VGAM1224 host target gene. FBXO21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO21 BINDING SITE, designated SEQ ID:27326, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43872] Another function of VGAM1224 is therefore inhibition of F-box Only Protein 21 (FBXO21, Accession NM_033624). Accordingly, utilities of VGAM1224 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with FBXO21. FLJ11715 (Accession NM_024564) is another VGAM1224 host target gene. FLJ11715 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ11715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11715 BINDING SITE, designated SEQ ID:23789, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43873] Another function of VGAM1224 is therefore inhibition of FLJ11715 (Accession NM_024564). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11715. FLJ11939 (Accession NM_024679) is another VGAM1224 host target gene. FLJ11939 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11939

BINDING SITE, designated SEQ ID:23990, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43874] Another function of VGAM1224 is therefore inhibition of FLJ11939 (Accession NM_024679). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11939. FLJ12619 (Accession NM_030939) is another VGAM1224 host target gene. FLJ12619 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12619 BINDING SITE, designated SEQ ID:25211, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43875] Another function of VGAM1224 is therefore inhibition of FLJ12619 (Accession NM_030939). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12619. FLJ12700 (Accession NM_024910) is another VGAM1224 host target gene. FLJ12700 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12700 BINDING SITE, designated SEQ ID:24416, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43876] Another function of VGAM1224 is therefore inhibition of FLJ12700 (Accession NM_024910). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12700. FLJ20739 (Accession XM_042197) is another VGAM1224 host target gene. FLJ20739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20739 BINDING SITE, designated SEQ ID:33704, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43877] Another function of VGAM1224 is therefore inhibition of

FLJ20739 (Accession XM_042197). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20739. FLJ21945 (Accession NM_025203) is another VGAM1224 host target gene. FLJ21945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21945 BINDING SITE, designated SEQ ID:24868, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43878] Another function of VGAM1224 is therefore inhibition of FLJ21945 (Accession NM_025203). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21945. FLJ30567 (Accession NM_145022) is another VGAM1224 host target gene. FLJ30567 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ30567 BINDING SITE, designated SEQ ID:29629, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43879] Another function of VGAM1224 is therefore inhibition of FLJ30567 (Accession NM_145022). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30567. KIAA0010 (Accession NM_014671) is another VGAM1224 host target gene. KIAA0010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0010 BINDING SITE, designated SEQ ID:16130, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43880] Another function of VGAM1224 is therefore inhibition of KIAA0010 (Accession NM_014671). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0010. KIAA0237 (Accession NM_014747) is another

VGAM1224 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16454, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43881] Another function of VGAM1224 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0426 (Accession NM_014724) is another VGAM1224 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16309, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43882] Another function of VGAM1224 is therefore inhibition of KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA0427 (Accession NM_014772) is another VGAM1224 host target gene. KIAA0427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0427 BINDING SITE, designated SEQ ID:16573, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43883] Another function of VGAM1224 is therefore inhibition of KIAA0427 (Accession NM_014772). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0427. KIAA0792 (Accession NM_014698) is another VGAM1224 host target gene. KIAA0792 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0792, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0792 BINDING SITE, designated SEQ ID:16215, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43884] Another function of VGAM1224 is therefore inhibition of KIAA0792 (Accession NM_014698). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0792. KIAA1052 (Accession NM_014956) is another VGAM1224 host target gene. KIAA1052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1052 BINDING SITE, designated SEQ ID:17310, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43885] Another function of VGAM1224 is therefore inhibition of KIAA1052 (Accession NM_014956). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1052. KIAA1205 (Accession XM_046305) is another VGAM1224 host target gene. KIAA1205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1205 BINDING SITE, designated SEQ ID:34705, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43886] Another function of VGAM1224 is therefore inhibition of KIAA1205 (Accession XM_046305). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1205. KIAA1322 (Accession XM_052626) is another VGAM1224 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36021, to the nucleotide sequence of VGAM1224 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3935.

[43887] Another function of VGAM1224 is therefore inhibition of KIAA1322 (Accession XM_052626). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1467 (Accession XM_049605) is another VGAM1224 host target gene. KIAA1467 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1467, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1467 BINDING SITE, designated SEQ ID:35452, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43888] Another function of VGAM1224 is therefore inhibition of KIAA1467 (Accession XM_049605). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1467. KIAA1674 (Accession XM_044065) is another VGAM1224 host target gene. KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1674, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34110, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43889] Another function of VGAM1224 is therefore inhibition of KIAA1674 (Accession XM_044065). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. KIAA1819 (Accession XM_045716) is another VGAM1224 host target gene. KIAA1819 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1819 BINDING SITE, designated SEQ ID:34536, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43890] Another function of VGAM1224 is therefore inhibition of KIAA1819 (Accession XM_045716). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1819. KIAA1918 (Accession XM_054951) is another VGAM1224 host target gene. KIAA1918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1918 BINDING SITE, designated SEQ ID:36218, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43891] Another function of VGAM1224 is therefore inhibition of KIAA1918 (Accession XM_054951). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1918. KIAA1949 (Accession XM_166376) is another VGAM1224 host target gene. KIAA1949 BINDING SITE1 through KIAA1949 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1949, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1949 BINDING SITE1 through

KIAA1949 BINDING SITE3, designated SEQ ID:44209, SEQ ID:46668 and SEQ ID:46713 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43892] Another function of VGAM1224 is therefore inhibition of KIAA1949 (Accession XM_166376). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1949. MGC16491 (Accession NM_052943) is another VGAM1224 host target gene. MGC16491 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC16491, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16491 BINDING SITE, designated SEQ ID:27502, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43893] Another function of VGAM1224 is therefore inhibition of MGC16491 (Accession NM_052943). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16491. Myosin XVIIIIB (MYO18B, Accession

NM_032608) is another VGAM1224 host target gene.

MYO18B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO18B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO18B BINDING SITE, designated SEQ ID:26332, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43894] Another function of VGAM1224 is therefore inhibition of Myosin XVIIIIB (MYO18B, Accession NM_032608). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO18B. Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_144498) is another VGAM1224 host target gene. OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OSBPL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2, desig-

nated SEQ ID:29319 and SEQ ID:16851 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43895] Another function of VGAM1224 is therefore inhibition of Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_144498). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL2. Phosphatase, Orphan 1 (phospho1, Accession XM_091572) is another VGAM1224 host target gene. phospho1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by phospho1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of phospho1 BINDING SITE, designated SEQ ID:40062, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43896] Another function of VGAM1224 is therefore inhibition of Phosphatase, Orphan 1 (phospho1, Accession XM_091572). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with phospho1. SDS3 (Accession

XM_045014) is another VGAM1224 host target gene. SDS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDS3 BINDING SITE, designated SEQ ID:34319, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43897] Another function of VGAM1224 is therefore inhibition of SDS3 (Accession XM_045014). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDS3. SIMRP7 (Accession XM_166462) is another VGAM1224 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44373, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43898] Another function of VGAM1224 is therefore inhibition of SIMRP7 (Accession XM_166462). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7. SP192 (Accession NM_021639) is another VGAM1224 host target gene. SP192 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SP192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP192 BINDING SITE, designated SEQ ID:22299, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43899] Another function of VGAM1224 is therefore inhibition of SP192 (Accession NM_021639). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP192. Stathmin-like 3 (STMN3, Accession NM_015894) is another VGAM1224 host target gene. STMN3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STMN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STMN3 BINDING SITE, designated SEQ ID:18039, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43900] Another function of VGAM1224 is therefore inhibition of Stathmin-like 3 (STMN3, Accession NM_015894). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STMN3. LOC126917 (Accession XM_059091) is another VGAM1224 host target gene. LOC126917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE, designated SEQ ID:36868, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43901] Another function of VGAM1224 is therefore inhibition of LOC126917 (Accession XM_059091). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC126917. LOC144114 (Accession XM_090198) is another VGAM1224 host target gene. LOC144114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144114 BINDING SITE, designated SEQ ID:39995, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43902] Another function of VGAM1224 is therefore inhibition of LOC144114 (Accession XM_090198). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144114. LOC144473 (Accession XM_096606) is another VGAM1224 host target gene. LOC144473 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144473, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144473 BINDING SITE, designated SEQ ID:40415, to the nucleotide sequence of VGAM1224 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3935.

[43903] Another function of VGAM1224 is therefore inhibition of LOC144473 (Accession XM_096606). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144473. LOC144866 (Accession XM_096699) is another VGAM1224 host target gene. LOC144866 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144866, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144866 BINDING SITE, designated SEQ ID:40478, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43904] Another function of VGAM1224 is therefore inhibition of LOC144866 (Accession XM_096699). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144866. LOC145815 (Accession XM_096874) is another VGAM1224 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145815, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145815 BINDING SITE, designated SEQ ID:40603, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43905] Another function of VGAM1224 is therefore inhibition of LOC145815 (Accession XM_096874). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. LOC146823 (Accession XM_097105) is another VGAM1224 host target gene. LOC146823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146823 BINDING SITE, designated SEQ ID:40750, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43906] Another function of VGAM1224 is therefore inhibition of LOC146823 (Accession XM_097105). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC146823. LOC153146 (Accession XM_098319) is another VGAM1224 host target gene. LOC153146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153146 BINDING SITE, designated SEQ ID:41577, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43907] Another function of VGAM1224 is therefore inhibition of LOC153146 (Accession XM_098319). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153146. LOC155072 (Accession XM_098661) is another VGAM1224 host target gene. LOC155072 BINDING SITE1 and LOC155072 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC155072, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155072 BINDING SITE1

and LOC155072 BINDING SITE2, designated SEQ ID:41759 and SEQ ID:41762 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43908] Another function of VGAM1224 is therefore inhibition of LOC155072 (Accession XM_098661). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155072. LOC202868 (Accession XM_117477) is another VGAM1224 host target gene. LOC202868 BINDING SITE1 and LOC202868 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC202868, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202868 BINDING SITE1 and LOC202868 BINDING SITE2, designated SEQ ID:43450 and SEQ ID:43024 respectively, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43909] Another function of VGAM1224 is therefore inhibition of LOC202868 (Accession XM_117477). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC202868. LOC221814 (Accession XM_168226) is another VGAM1224 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45097, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43910] Another function of VGAM1224 is therefore inhibition of LOC221814 (Accession XM_168226). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. LOC254532 (Accession XM_172961) is another VGAM1224 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46214, to

the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43911] Another function of VGAM1224 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC89944 (Accession XM_166198) is another VGAM1224 host target gene. LOC89944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89944 BINDING SITE, designated SEQ ID:44004, to the nucleotide sequence of VGAM1224 RNA, herein designated VGAM RNA, also designated SEQ ID:3935.

[43912] Another function of VGAM1224 is therefore inhibition of LOC89944 (Accession XM_166198). Accordingly, utilities of VGAM1224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89944. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1225 (VGAM1225) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43913] VGAM1225 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1225 was detected is described hereinabove with reference to Figs. 1–8.

[43914] VGAM1225 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 1. VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43915] VGAM1225 gene encodes a VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1225 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1225 precursor RNA is designated SEQ ID:1211, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1211 is located at position 88490 relative to the genome of Human Herpesvirus 1.

[43916] VGAM1225 precursor RNA folds onto itself, forming VGAM1225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43917] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1225 folded precursor RNA into VGAM1225 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1225 RNA is designated SEQ ID:3936, and is provided hereinbelow with reference to the sequence listing part.

[43918] VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1225 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1225 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43919] VGAM1225 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1225 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1225 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43920] The complementary binding of VGAM1225 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1225 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1225 host target RNA into VGAM1225 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43921] It is appreciated that VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1225 host target genes. The mRNA of each one of this plurality of VGAM1225 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1225 RNA, herein designated VGAM RNA, and which when bound by VGAM1225 RNA causes inhibition of translation of respective one or more VGAM1225 host target proteins.

[43922] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1225 gene, herein designated VGAM GENE, on one or more VGAM1225 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43923] It is yet further appreciated that a function of VGAM1225 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1225 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1225 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43924] Nucleotide sequences of the VGAM1225 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1225 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1225 are further described hereinbelow with reference to Table 1.

[43925] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1225 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1225 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43926] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1225 gene, herein designated VGAM is inhibition of expression of VGAM1225 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1225 correlate with, and may be deduced from, the identity of the target genes which VGAM1225

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43927] Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM_002235) is a VGAM1225 host target gene. KCNA6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA6 BINDING SITE, designated SEQ ID:8016, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43928] A function of VGAM1225 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 6 (KCNA6, Accession NM_002235), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNA6. The function of KCNA6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM893. Maltase–glucoamylase (alpha–glucosidase) (MGAM, Accession XM_051351) is another VGAM1225 host target gene. MGAM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAM BINDING SITE, designated SEQ ID:35823, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43929] Another function of VGAM1225 is therefore inhibition of Maltase–glucoamylase (alpha–glucosidase) (MGAM, Accession XM_051351), a gene which plays a role in the final steps of digestion of starch. Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAM. The function of MGAM and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM791. C16orf5 (Accession NM_013399) is another VGAM1225 host target gene. C16orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by C16orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C16orf5 BINDING SITE, designated SEQ ID:15056, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43930] Another function of VGAM1225 is therefore inhibition of C16orf5 (Accession NM_013399). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C16orf5. KIAA1303 (Accession XM_038376) is another VGAM1225 host target gene. KIAA1303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1303 BINDING SITE, designated SEQ ID:32833, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43931] Another function of VGAM1225 is therefore inhibition of KIAA1303 (Accession XM_038376). Accordingly, utilities

of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1303. NFASC (Accession XM_046808) is another VGAM1225 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34829, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43932] Another function of VGAM1225 is therefore inhibition of NFASC (Accession XM_046808). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. NIR3 (Accession XM_038799) is another VGAM1225 host target gene. NIR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIR3 BINDING SITE, designated SEQ

ID:32925, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43933] Another function of VGAM1225 is therefore inhibition of NIR3 (Accession XM_038799). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIR3. NYD-SP25 (Accession NM_033516) is another VGAM1225 host target gene. NYD-SP25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NYD-SP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP25 BINDING SITE, designated SEQ ID:27294, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43934] Another function of VGAM1225 is therefore inhibition of NYD-SP25 (Accession NM_033516). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP25. LOC132422 (Accession XM_067839) is another VGAM1225 host target gene. LOC132422 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC132422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132422 BINDING SITE, designated SEQ ID:37369, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43935] Another function of VGAM1225 is therefore inhibition of LOC132422 (Accession XM_067839). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132422. LOC143915 (Accession XM_096502) is another VGAM1225 host target gene. LOC143915 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143915 BINDING SITE, designated SEQ ID:40376, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43936] Another function of VGAM1225 is therefore inhibition of

LOC143915 (Accession XM_096502). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143915. LOC151178 (Accession XM_087117) is another VGAM1225 host target gene. LOC151178 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151178 BINDING SITE, designated SEQ ID:39070, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43937] Another function of VGAM1225 is therefore inhibition of LOC151178 (Accession XM_087117). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151178. LOC166042 (Accession XM_093623) is another VGAM1225 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40197, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43938] Another function of VGAM1225 is therefore inhibition of LOC166042 (Accession XM_093623). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC196759 (Accession XM_113601) is another VGAM1225 host target gene. LOC196759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196759 BINDING SITE, designated SEQ ID:42293, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43939] Another function of VGAM1225 is therefore inhibition of LOC196759 (Accession XM_113601). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196759. LOC197201 (Accession XM_113839) is an-

other VGAM1225 host target gene. LOC197201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197201 BINDING SITE, designated SEQ ID:42460, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43940] Another function of VGAM1225 is therefore inhibition of LOC197201 (Accession XM_113839). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197201. LOC254755 (Accession XM_173224) is another VGAM1225 host target gene. LOC254755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254755 BINDING SITE, designated SEQ ID:46486, to the nucleotide sequence of VGAM1225 RNA, herein designated VGAM RNA, also designated SEQ ID:3936.

[43941] Another function of VGAM1225 is therefore inhibition of LOC254755 (Accession XM_173224). Accordingly, utilities of VGAM1225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254755. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1226 (VGAM1226) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43942] VGAM1226 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1226 was detected is described hereinabove with reference to Figs. 1–8.

[43943] VGAM1226 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tacaribe Virus.

VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43944] VGAM1226 gene encodes a VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1226 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1226 precursor RNA is designated SEQ ID:1212, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1212 is located at position 6654 relative to the genome of Tacaribe Virus.

[43945] VGAM1226 precursor RNA folds onto itself, forming VGAM1226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43946] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1226 folded precursor RNA into VGAM1226 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 64%) nucleotide sequence of VGAM1226 RNA is designated SEQ ID:3937, and is provided hereinbelow with reference to the sequence listing part.

[43947] VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1226 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43948] VGAM1226 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1226 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1226 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43949] The complementary binding of VGAM1226 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1226 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1226 host target RNA into VGAM1226 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43950] It is appreciated that VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1226 host target genes. The mRNA of each one of this plurality of VGAM1226 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1226 RNA, herein designated VGAM RNA, and which when bound by VGAM1226 RNA causes inhibition of translation of respective one or more VGAM1226 host target proteins.

[43951] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1226 gene, herein designated VGAM GENE, on one or more VGAM1226 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43952] It is yet further appreciated that a function of VGAM1226 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of viral infection by Tacaribe Virus. Specific functions, and accordingly utilities, of VGAM1226 correlate with, and may be deduced from, the identity of the host target genes which VGAM1226 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43953] Nucleotide sequences of the VGAM1226 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1226 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1226 are further described hereinbelow with reference to Table 1.

[43954] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1226 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1226 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[43955] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1226 gene, herein designated VGAM is inhibition of expression of VGAM1226 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1226 correlate with, and may be deduced from, the identity of the target genes which VGAM1226 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43956] Archain 1 (ARCN1, Accession NM_001655) is a VGAM1226 host target gene. ARCN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARCN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARCN1 BINDING SITE, designated SEQ ID:7364, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43957] A function of VGAM1226 is therefore inhibition of Archain 1 (ARCN1, Accession NM_001655), a gene which plays a fundamental role in eukaryotic cell biology. Accordingly, utilities of VGAM1226 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with ARCN1. The function of ARCN1 has been established by previous studies. Radice et al. (1995) identified a gene that maps approximately 50-kb telomeric to MLL (OMIM Ref. No. 159555) in band 11q23.3, a locus disrupted in certain leukemia-associated translocation chromosomes. A 200-kb genomic fragment from a YAC that includes MLL was used to screen a cDNA library of the R54;11 cell line which carries a translocation chromosome t(4;11)(q21; q23). The cDNA sequence predicts a 511-amino acid protein which shares similarity with predicted proteins of unknown function from rice (*Oryza sativa*) and *Drosophila*. Because of this ancient conservation the authors proposed the name archain (ARCN1). Radice et al. (1995) detected 4-kb ARCN1 transcripts by Northern blot analysis in all tissues examined. The protein encoded by the ARCN1 gene, the coatomer protein delta-COP, probably plays a fundamental role in eukaryotic cell biology. Tunnacliffe et al. (1996) demonstrated that it is conserved across diverse eukaryotes. Very close or identical matches were seen in rat and cow; highly significant matches were seen with 2 plant species, *A. thaliana* (cress) and *S. tuberosum* (OMIM Ref. No. potato). Of particular bi-

ologic significance was the match with a sequence on yeast chromosome VI, from which Tunnacliffe et al. (1996) were able to determine the yeast archain gene and protein sequence. Unpublished data indicated that in situ hybridizations on mouse embryo sections showed archain transcripts throughout the whole animal.

[43958] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[43959] Radice, P.; Pensotti, V.; Jones, C.; Perry, H.; Pierotti, M. A.; Tunnacliffe, A. : The human archain gene, ARCN1, has highly conserved homologs in rice and Drosophila. *Genomics* 26: 101–106, 1995. ; and

[43960] Tunnacliffe, A.; van de Vrugt, H.; Pensotti, V.; Radice, P. : The coatomer protein delta-COP, encoded by the archain gene, is conserved across diverse eukaryotes. *Mammalian Genome* 7: 78.

[43961] Further studies establishing the function and utilities of ARCN1 are found in John Hopkins OMIM database record ID 600820, and in cited publications numbered 7529–7530 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin D2 (CCND2, Accession NM_001759) is another VGAM1226

host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7510, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43962] Another function of VGAM1226 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the G1/S (start) transition. Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Leukemia Inhibitory Factor Receptor (LIFR, Accession NM_002310) is another VGAM1226 host target gene. LIFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIFR, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIFR BINDING SITE, designated SEQ ID:8098, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43963] Another function of VGAM1226 is therefore inhibition of Leukemia Inhibitory Factor Receptor (LIFR, Accession NM_002310). Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIFR. C-myc Binding Protein (MYCBP, Accession NM_012333) is another VGAM1226 host target gene. MYCBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCBP BINDING SITE, designated SEQ ID:14724, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43964] Another function of VGAM1226 is therefore inhibition of C-myc Binding Protein (MYCBP, Accession NM_012333), a gene which binds c-Myc stimulating the activation of E-

box-dependent transcription. Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCBP. The function of MYCBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM435. Tryptophanyl-tRNA Synthetase (WARS, Accession XM_041014) is another VGAM1226 host target gene. WARS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WARS BINDING SITE, designated SEQ ID:33412, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43965] Another function of VGAM1226 is therefore inhibition of Tryptophanyl-tRNA Synthetase (WARS, Accession XM_041014), a gene which is a tryptophanyl-tRNA synthetase. Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WARS. The function of WARS and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM68.KLK15 (Accession NM_023006) is another VGAM1226 host target gene. KLK15 BINDING SITE1 and KLK15 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK15, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK15 BINDING SITE1 and KLK15 BINDING SITE2, designated SEQ ID:23262 and SEQ ID:28860 respectively, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43966] Another function of VGAM1226 is therefore inhibition of KLK15 (Accession NM_023006). Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK15. LOC132241 (Accession XM_059583) is another VGAM1226 host target gene. LOC132241 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC132241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC132241 BINDING SITE, designated SEQ ID:37022, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43967] Another function of VGAM1226 is therefore inhibition of LOC132241 (Accession XM_059583). Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132241. LOC158434 (Accession XM_098939) is another VGAM1226 host target gene. LOC158434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158434 BINDING SITE, designated SEQ ID:41984, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43968] Another function of VGAM1226 is therefore inhibition of LOC158434 (Accession XM_098939). Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158434. LOC158549 (Accession XM_098963) is an-

other VGAM1226 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42008, to the nucleotide sequence of VGAM1226 RNA, herein designated VGAM RNA, also designated SEQ ID:3937.

[43969] Another function of VGAM1226 is therefore inhibition of LOC158549 (Accession XM_098963). Accordingly, utilities of VGAM1226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1227 (VGAM1227) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43970] VGAM1227 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1227 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[43971] VGAM1227 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tacaribe Virus.

VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43972] VGAM1227 gene encodes a VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1227 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1227 precursor RNA is designated SEQ ID:1213, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1213 is located at position 1706 relative to the genome of Tacaribe Virus.

[43973] VGAM1227 precursor RNA folds onto itself, forming VGAM1227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43974] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1227 folded precursor RNA into VGAM1227 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1227 RNA is designated SEQ ID:3938, and is provided hereinbelow with reference to the sequence listing part.

[43975] VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1227 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43976] VGAM1227 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1227 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1227 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1227 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43977] The complementary binding of VGAM1227 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1227 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1227 host target RNA into VGAM1227 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43978] It is appreciated that VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1227 host target genes. The mRNA of each one of this plurality of VGAM1227 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1227 RNA, herein designated VGAM RNA, and which when bound by VGAM1227 RNA causes inhibition of translation of respective one or more VGAM1227 host target proteins.

[43979] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1227 gene, herein designated VGAM GENE, on one or more VGAM1227 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43980] It is yet further appreciated that a function of VGAM1227 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1227 include diagnosis, prevention and treatment of viral infection by Tacaribe Virus. Specific functions, and accordingly utilities, of VGAM1227 correlate with, and may be deduced from, the identity of the host target genes which VGAM1227 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43981] Nucleotide sequences of the VGAM1227 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1227 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1227 are further described hereinbelow with reference to Table 1.

[43982] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1227 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1227 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43983] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1227 gene, herein designated VGAM is inhibition of expression of VGAM1227 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1227 correlate with, and may be deduced from, the identity of the target genes which VGAM1227 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[43984] Hexokinase 1 (HK1, Accession NM_033497) is a VGAM1227 host target gene. HK1 BINDING SITE1 through HK1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HK1, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HK1 BINDING SITE1 through HK1 BINDING SITE3, designated SEQ ID:27268, SEQ ID:27274 and SEQ ID:27271 respectively, to the nucleotide sequence of VGAM1227 RNA, herein designated VGAM RNA, also designated SEQ ID:3938.

[43985] A function of VGAM1227 is therefore inhibition of Hexokinase 1 (HK1, Accession NM_033497). Accordingly, utilities of VGAM1227 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HK1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1228 (VGAM1228) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[43986] VGAM1228 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1228 was detected is described hereinabove with reference to Figs. 1-8.

[43987] VGAM1228 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Tacaribe Virus.

VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[43988] VGAM1228 gene encodes a VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1228 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1228 precursor RNA is designated SEQ ID:1214, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1214 is located at position 2505 relative to the genome of Tacaribe Virus.

[43989] VGAM1228 precursor RNA folds onto itself, forming VGAM1228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[43990] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1228 folded precursor RNA into VGAM1228 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1228 RNA is designated SEQ ID:3939, and is provided hereinbelow with reference to the sequence listing part.

[43991] VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1228 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[43992] VGAM1228 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1228 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1228 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[43993] The complementary binding of VGAM1228 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1228 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1228

host target RNA into VGAM1228 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[43994] It is appreciated that VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1228 host target genes. The mRNA of each one of this plurality of VGAM1228 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1228 RNA, herein designated VGAM RNA, and which when bound by VGAM1228 RNA causes inhibition of translation of respective one or more VGAM1228 host target proteins.

[43995] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1228 gene, herein designated VGAM GENE, on one or more VGAM1228 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[43996] It is yet further appreciated that a function of VGAM1228 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of viral infection by Tacaribe Virus. Specific functions, and accordingly utilities, of VGAM1228 correlate with, and may be deduced from, the identity of the host target genes which VGAM1228 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[43997] Nucleotide sequences of the VGAM1228 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1228 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1228 are further

described hereinbelow with reference to Table 1.

[43998] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1228 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1228 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[43999] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1228 gene, herein designated VGAM is inhibition of expression of VGAM1228 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1228 correlate with, and may be deduced from, the identity of the target genes which VGAM1228 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44000] Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM_001408) is a VGAM1228 host target gene. CELSR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CELSR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of CELSR2 BINDING SITE, designated SEQ ID:7106, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44001] A function of VGAM1228 is therefore inhibition of Cadherin, EGF LAG Seven-pass G-type Receptor 2 (flamingo homolog, Drosophila) (CELSR2, Accession NM_001408), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CELSR2. The function of CELSR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. ERAP140 (Accession XM_059748) is another VGAM1228 host target gene. ERAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERAP140 BINDING SITE, designated SEQ ID:37085, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ

ID:3939.

[44002] Another function of VGAM1228 is therefore inhibition of ERAP140 (Accession XM_059748). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERAP140. FLJ13910 (Accession NM_022780) is another VGAM1228 host target gene. FLJ13910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13910 BINDING SITE, designated SEQ ID:23055, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44003] Another function of VGAM1228 is therefore inhibition of FLJ13910 (Accession NM_022780). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13910. HCA127 (Accession NM_018684) is another VGAM1228 host target gene. HCA127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA127, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA127 BINDING SITE, designated SEQ ID:20759, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44004] Another function of VGAM1228 is therefore inhibition of HCA127 (Accession NM_018684). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA127. KIAA1009 (Accession NM_014895) is another VGAM1228 host target gene. KIAA1009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1009 BINDING SITE, designated SEQ ID:17052, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44005] Another function of VGAM1228 is therefore inhibition of KIAA1009 (Accession NM_014895). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1009. Kv6.3 (Accession NM_133490) is another VGAM1228 host target gene. Kv6.3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Kv6.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Kv6.3 BINDING SITE, designated SEQ ID:28566, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44006] Another function of VGAM1228 is therefore inhibition of Kv6.3 (Accession NM_133490). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Kv6.3. PRO0365 (Accession NM_014126) is another VGAM1228 host target gene. PRO0365 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0365, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0365 BINDING SITE, designated SEQ ID:15389, to the nucleotide sequence of

VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44007] Another function of VGAM1228 is therefore inhibition of PRO0365 (Accession NM_014126). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0365. LOC152742 (Accession XM_098259) is another VGAM1228 host target gene. LOC152742 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152742 BINDING SITE, designated SEQ ID:41544, to the nucleotide sequence of VGAM1228 RNA, herein designated VGAM RNA, also designated SEQ ID:3939.

[44008] Another function of VGAM1228 is therefore inhibition of LOC152742 (Accession XM_098259). Accordingly, utilities of VGAM1228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152742. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1229 (VGAM1229) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44009] VGAM1229 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1229 was detected is described hereinabove with reference to Figs. 1–8.

[44010] VGAM1229 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tacaribe Virus. VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44011] VGAM1229 gene encodes a VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1229 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1229 precursor RNA is designated SEQ ID:1215, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1215 is located at position 2314 relative to the genome of Tacaribe Virus.

[44012] VGAM1229 precursor RNA folds onto itself, forming VGAM1229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44013] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1229 folded precursor RNA into VGAM1229 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM1229 RNA is designated SEQ ID:3940, and is provided hereinbelow with reference to the sequence listing part.

[44014] VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1229 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1229 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44015] VGAM1229 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1229 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1229 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44016] The complementary binding of VGAM1229 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1229 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1229 host target RNA into VGAM1229 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44017] It is appreciated that VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1229 host target genes. The mRNA of each one of this plurality of VGAM1229 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1229 RNA, herein designated VGAM RNA, and which when bound by VGAM1229 RNA causes inhibition of translation of respective one or more VGAM1229 host target proteins.

[44018] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1229 gene, herein designated VGAM GENE, on one or more VGAM1229 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44019] It is yet further appreciated that a function of VGAM1229 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of viral infection by Tacaribe Virus. Specific functions, and accordingly utilities, of VGAM1229 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1229 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44020] Nucleotide sequences of the VGAM1229 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1229 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1229 are further described hereinbelow with reference to Table 1.

[44021] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1229 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1229 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44022] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1229 gene, herein designated VGAM is inhibition of expression of VGAM1229 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1229 correlate with, and may be deduced from, the identity of the target genes which VGAM1229

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44023] Cysteine-rich, Angiogenic Inducer, 61 (CYR61, Accession NM_001554) is a VGAM1229 host target gene. CYR61 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYR61, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYR61 BINDING SITE, designated SEQ ID:7276, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44024] A function of VGAM1229 is therefore inhibition of Cysteine-rich, Angiogenic Inducer, 61 (CYR61, Accession NM_001554), a gene which promotes the adhesion of endothelial cells. Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYR61. The function of CYR61 has been established by previous studies. CYR61 is a secreted, cysteine-rich, heparin-binding protein encoded by a growth factor-inducible immediate-early gene. Acting as an extracellular, matrix-associated signaling molecule, CYR61 promotes the adhesion of endothelial

cells through interaction with integrin and augments growth factor-induced DNA synthesis in the same cell type. Babic et al. (1998) showed that purified CYR61 stimulates directed migration of human microvascular endothelial cells in culture through the $\alpha(V)\beta(3)$ -dependent pathway and induces neovascularization in rat corneas. Both the chemotactic and angiogenic activities of CYR61 can be blocked by specific anti-CYR61 antibodies. Whereas most human tumor-derived cell lines tested expressed CYR61, a gastric adenocarcinoma cell line did not. Expression of the CYR61 cDNA under the regulation of a constitutive promoter from this gastric cancer cell line significantly enhanced the tumorigenicity of these cells as measured by growth in immunodeficient mice, resulting in tumors that were larger and more vascularized than those produced by control cells. Taken together, these results identified CYR61 as an angiogenic inducer that can promote tumor growth and vascularization; the results also suggested to Babic et al. (1998) potential roles for CYR61 in physiologic and pathologic neovascularization. Sampath et al. (2001) used rapid analysis of differential expression (RADE) to identify genes that are abnormally expressed in leiomyomas. Of

the several genes identified, CYR61, a member of the CCN family of growth and angiogenic regulators, was shown to be markedly downregulated at the mRNA and protein levels in leiomyoma tumors compared with the 38 matched uterine myometrial controls. In addition, in situ hybridization experiments corroborated the lack of CYR61 expression in leiomyoma cells, whereas abundant transcript levels were identified in adjacent myometrial smooth muscle cells. To elucidate the mechanisms of CYR61 gene regulation in leiomyomas, they determined the effects of ovarian steroids, basic fibroblast growth factor (FGFB; 134920), and serum on CYR61 expression using an ex vivo culture system. Treatment of human myometrial explants with 17-beta-estradiol and FGFB upregulated CYR61 transcripts. Paradoxically, neither 17-beta-estradiol nor FGFB was capable of upregulating CYR61 mRNA in leiomyoma explants despite elevated levels of ESRA (OMIM Ref. No. 133430) mRNA. The authors concluded that dysregulation of CYR61 by estrogen and FGFB may contribute to downregulation of CYR61 in leiomyomas which, in turn, may predispose uterine smooth muscle cells toward sustained growth.

[44025] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [44026] Babic, A. M.; Kireeva, M. L.; Kolesnikova, T. V.; Lau, L. F. : CYR61, a product of a growth factor-inducible immediate early gene, promotes angiogenesis and tumor growth. Proc. Nat. Acad. Sci. 95: 6355–6360, 1998. ; and
- [44027] Sampath, D.; Zhu, Y.; Winneker, R. C.; Zhang, Z. : Aberrant expression of Cyr61, a member of the CCN (CTGF/Cyr61/Cef10/NOVH) family, and dysregulation by 17-beta-estradiol and basic fibr.
- [44028] Further studies establishing the function and utilities of CYR61 are found in John Hopkins OMIM database record ID 602369, and in cited publications numbered 8934–893 and 11958–8938 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM1229 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ

ID:32195, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44029] Another function of VGAM1229 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Nuclear Factor (erythroid-derived 2)-like 1 (NFE2L1, Accession NM_003204) is another VGAM1229 host target gene. NFE2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFE2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFE2L1 BINDING SITE, designated SEQ ID:9198, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44030] Another function of VGAM1229 is therefore inhibition of Nuclear Factor (erythroid-derived 2)-like 1 (NFE2L1, Accession NM_003204), a gene which may regulate expression of ferritin genes. Accordingly, utilities of VGAM1229

include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFE2L1. The function of NFE2L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM369. Tropomodulin 2 (neuronal) (TMOD2, Accession NM_014548) is another VGAM1229 host target gene. TMOD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMOD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMOD2 BINDING SITE, designated SEQ ID:15859, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44031] Another function of VGAM1229 is therefore inhibition of Tropomodulin 2 (neuronal) (TMOD2, Accession NM_014548), a gene which is an actin-capping protein for the slow-growing end of filamentous actin. Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMOD2. The function of TMOD2 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM791. ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949) is another VGAM1229 host target gene.

ACTR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1A BINDING SITE, designated SEQ ID:31533, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44032] Another function of VGAM1229 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR1A. Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM_029741) is another VGAM1229 host target gene. C20orf130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by C20orf130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf130 BINDING SITE, designated SEQ ID:30934, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44033] Another function of VGAM1229 is therefore inhibition of Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM_029741). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf130. FLJ22087 (Accession NM_022070) is another VGAM1229 host target gene. FLJ22087 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22087 BINDING SITE, designated SEQ ID:22613, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44034] Another function of VGAM1229 is therefore inhibition of

FLJ22087 (Accession NM_022070). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22087. KIAA0940 (Accession NM_014912) is another VGAM1229 host target gene. KIAA0940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0940 BINDING SITE, designated SEQ ID:17148, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44035] Another function of VGAM1229 is therefore inhibition of KIAA0940 (Accession NM_014912). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0940. KIAA1463 (Accession XM_051160) is another VGAM1229 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35771, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44036] Another function of VGAM1229 is therefore inhibition of KIAA1463 (Accession XM_051160). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. MGC2541 (Accession NM_080670) is another VGAM1229 host target gene. MGC2541 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2541, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2541 BINDING SITE, designated SEQ ID:27963, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44037] Another function of VGAM1229 is therefore inhibition of MGC2541 (Accession NM_080670). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2541. MIL1 (Accession NM_015367) is another

VGAM1229 host target gene. MIL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIL1 BINDING SITE, designated SEQ ID:17665, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44038] Another function of VGAM1229 is therefore inhibition of MIL1 (Accession NM_015367). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIL1. Mucin 17 (MUC17, Accession XM_168583) is another VGAM1229 host target gene. MUC17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MUC17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC17 BINDING SITE, designated SEQ ID:45259, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44039] Another function of VGAM1229 is therefore inhibition of Mucin 17 (MUC17, Accession XM_168583). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC17. PRO1257 (Accession NM_018578) is another VGAM1229 host target gene. PRO1257 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1257 BINDING SITE, designated SEQ ID:20656, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44040] Another function of VGAM1229 is therefore inhibition of PRO1257 (Accession NM_018578). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1257. Ring Finger Protein 2 (RNF2, Accession NM_007212) is another VGAM1229 host target gene. RNF2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF2, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF2 BINDING SITE, designated SEQ ID:14074, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44041] Another function of VGAM1229 is therefore inhibition of Ring Finger Protein 2 (RNF2, Accession NM_007212). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF2. LOC164397 (Accession XM_092780) is another VGAM1229 host target gene. LOC164397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164397 BINDING SITE, designated SEQ ID:40147, to the nucleotide sequence of VGAM1229 RNA, herein designated VGAM RNA, also designated SEQ ID:3940.

[44042] Another function of VGAM1229 is therefore inhibition of LOC164397 (Accession XM_092780). Accordingly, utilities of VGAM1229 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC164397. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1230 (VGAM1230) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44043] VGAM1230 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1230 was detected is described hereinabove with reference to Figs. 1–8.

[44044] VGAM1230 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44045] VGAM1230 gene encodes a VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1230 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1230 precursor RNA is desig-

nated SEQ ID:1216, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1216 is located at position 12219 relative to the genome of Equine Herpesvirus 2.

- [44046] VGAM1230 precursor RNA folds onto itself, forming VGAM1230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44047] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1230 folded precursor RNA into VGAM1230 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1230 RNA is designated SEQ ID:3941, and is provided hereinbelow with reference to the sequence

listing part.

[44048] VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1230 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44049] VGAM1230 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1230 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1230 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44050] The complementary binding of VGAM1230 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1230 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1230 host target RNA into VGAM1230 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44051] It is appreciated that VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1230 host target genes. The mRNA of each one of this plurality of VGAM1230 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1230 RNA, herein designated VGAM

RNA, and which when bound by VGAM1230 RNA causes inhibition of translation of respective one or more VGAM1230 host target proteins.

[44052] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1230 gene, herein designated VGAM GENE, on one or more VGAM1230 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44053] It is yet further appreciated that a function of VGAM1230 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1230 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1230 correlate with, and may be deduced from, the identity of the host target genes which VGAM1230 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44054] Nucleotide sequences of the VGAM1230 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1230 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1230 are further described hereinbelow with reference to Table 1.

[44055] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1230 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1230 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44056] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1230 gene, herein designated VGAM is

inhibition of expression of VGAM1230 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1230 correlate with, and may be deduced from, the identity of the target genes which VGAM1230 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44057] Acid Phosphatase 2, Lysosomal (ACP2, Accession NM_001610) is a VGAM1230 host target gene. ACP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP2 BINDING SITE, designated SEQ ID:7318, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44058] A function of VGAM1230 is therefore inhibition of Acid Phosphatase 2, Lysosomal (ACP2, Accession NM_001610). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP2. Agrin (AGRN, Accession XM_086178) is another VGAM1230 host target gene. AGRN BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by AGRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGRN BINDING SITE, designated SEQ ID:38536, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44059] Another function of VGAM1230 is therefore inhibition of Agrin (AGRN, Accession XM_086178), a gene which a neuronal aggregating factor that induces the aggregation of acetylcholine receptors . Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGRN. The function of AGRN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1063.E2F Transcription Factor 3 (E2F3, Accession NM_001949) is another VGAM1230 host target gene. E2F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

E2F3 BINDING SITE, designated SEQ ID:7664, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44060] Another function of VGAM1230 is therefore inhibition of E2F Transcription Factor 3 (E2F3, Accession NM_001949), a gene which binds dna and controls cell-cycle progression from g1 to s phase. Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F3. The function of E2F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475.LIM Domains Containing 1 (LIMD1, Accession NM_014240) is another VGAM1230 host target gene. LIMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMD1 BINDING SITE, designated SEQ ID:15502, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44061] Another function of VGAM1230 is therefore inhibition of LIM Domains Containing 1 (LIMD1, Accession NM_014240). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMD1. Neurocalcin Delta (NCALD, Accession NM_032041) is another VGAM1230 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25745, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44062] Another function of VGAM1230 is therefore inhibition of Neurocalcin Delta (NCALD, Accession NM_032041). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. SH3 and Multiple Ankyrin Repeat Domains 2 (SHANK2, Accession NM_012309) is another VGAM1230 host target gene. SHANK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SHANK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHANK2 BINDING SITE, designated SEQ ID:14684, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44063] Another function of VGAM1230 is therefore inhibition of SH3 and Multiple Ankyrin Repeat Domains 2 (SHANK2, Accession NM_012309). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHANK2. Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM_005069) is another VGAM1230 host target gene. SIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM2 BINDING SITE, designated SEQ ID:11516, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44064] Another function of VGAM1230 is therefore inhibition of

Single-minded Homolog 2 (Drosophila) (SIM2, Accession NM_005069), a gene which may be a master gene of CNS development. Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM2. The function of SIM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM369. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184) is another VGAM1230 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31303, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44065] Another function of VGAM1230 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SPON1. DKFZP564L0864 (Accession XM_051905) is another VGAM1230 host target gene. DKFZP564L0864 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564L0864, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564L0864 BINDING SITE, designated SEQ ID:35919, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44066] Another function of VGAM1230 is therefore inhibition of DKFZP564L0864 (Accession XM_051905). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564L0864. DKFZp761B1514 (Accession NM_032288) is another VGAM1230 host target gene. DKFZp761B1514 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp761B1514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZp761B1514 BINDING SITE, designated SEQ ID:26047, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44067] Another function of VGAM1230 is therefore inhibition of DKFZp761B1514 (Accession NM_032288). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B1514. F-box Only Protein 9 (FBXO9, Accession NM_033480) is another VGAM1230 host target gene. FBXO9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO9 BINDING SITE, designated SEQ ID:27258, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44068] Another function of VGAM1230 is therefore inhibition of F-box Only Protein 9 (FBXO9, Accession NM_033480). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with FBXO9. KDEL (Lys–Asp–Glu–Leu) Endoplasmic Reticulum Protein Retention Receptor 3 (KDEL3, Accession NM_006855) is another VGAM1230 host target gene. KDEL3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KDEL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KDEL3 BINDING SITE, designated SEQ ID:13724, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44069] Another function of VGAM1230 is therefore inhibition of KDEL (Lys–Asp–Glu–Leu) Endoplasmic Reticulum Protein Retention Receptor 3 (KDEL3, Accession NM_006855). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KDEL3. KIAA0914 (Accession NM_014883) is another VGAM1230 host target gene. KIAA0914 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0914 BINDING SITE, designated SEQ ID:17034, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44070] Another function of VGAM1230 is therefore inhibition of KIAA0914 (Accession NM_014883). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0914. SKIP (Accession NM_130766) is another VGAM1230 host target gene. SKIP BINDING SITE1 and SKIP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SKIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIP BINDING SITE1 and SKIP BINDING SITE2, designated SEQ ID:28264 and SEQ ID:18600 respectively, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44071] Another function of VGAM1230 is therefore inhibition of SKIP (Accession NM_130766). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SKIP. LOC146856 (Accession XM_096086) is another VGAM1230 host target gene. LOC146856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146856 BINDING SITE, designated SEQ ID:40297, to the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44072] Another function of VGAM1230 is therefore inhibition of LOC146856 (Accession XM_096086). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146856. LOC200609 (Accession XM_117256) is another VGAM1230 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43321, to

the nucleotide sequence of VGAM1230 RNA, herein designated VGAM RNA, also designated SEQ ID:3941.

[44073] Another function of VGAM1230 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM1230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1231 (VGAM1231) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44074] VGAM1231 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1231 was detected is described hereinabove with reference to Figs. 1–8.

[44075] VGAM1231 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44076] VGAM1231 gene encodes a VGAM1231 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1231 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1231 precursor RNA is designated SEQ ID:1217, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1217 is located at position 10445 relative to the genome of Equine Herpesvirus 2.

[44077] VGAM1231 precursor RNA folds onto itself, forming VGAM1231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44078] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1231 folded precursor RNA into VGAM1231 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1231 RNA is designated SEQ ID:3942, and is provided hereinbelow with reference to the sequence listing part.

[44079] VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1231 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44080] VGAM1231 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1231 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1231 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44081] The complementary binding of VGAM1231 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1231 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1231 host target RNA into VGAM1231 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44082] It is appreciated that VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1231 host target genes. The mRNA of each one of this plurality of VGAM1231 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1231 RNA, herein designated VGAM RNA, and which when bound by VGAM1231 RNA causes inhibition of translation of respective one or more VGAM1231 host target proteins.

[44083] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1231 gene, herein designated VGAM GENE, on one or more VGAM1231 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[44084] It is yet further appreciated that a function of VGAM1231 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1231 correlate with, and may be deduced from, the identity of the host target genes which VGAM1231 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44085] Nucleotide sequences of the VGAM1231 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1231 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1231 are further described hereinbelow with reference to Table 1.

[44086] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1231 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1231 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44087] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1231 gene, herein designated VGAM is inhibition of expression of VGAM1231 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1231 correlate with, and may be deduced from, the identity of the target genes which VGAM1231 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44088] Extracellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM_001393) is a VGAM1231 host target gene. ECM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ECM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ECM2 BINDING SITE, designated SEQ ID:7087, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44089] A function of VGAM1231 is therefore inhibition of Extra-

cellular Matrix Protein 2, Female Organ and Adipocyte Specific (ECM2, Accession NM_001393). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ECM2. Muscleblind-like (Drosophila) (MBNL, Accession NM_021038) is another VGAM1231 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBNL BINDING SITE, designated SEQ ID:22031, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44090] Another function of VGAM1231 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM95.Parkinson Disease (autosomal recessive, juvenile) 2, Parkin (PARK2, Accession NM_013988) is another VGAM1231 host target gene. PARK2 BINDING SITE1 through PARK2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PARK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PARK2 BINDING SITE1 through PARK2 BINDING SITE3, designated SEQ ID:15161, SEQ ID:10907 and SEQ ID:15154 respectively, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44091] Another function of VGAM1231 is therefore inhibition of Parkinson Disease (autosomal recessive, juvenile) 2, Parkin (PARK2, Accession NM_013988). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PARK2. DKFZP434L187 (Accession XM_044070) is another VGAM1231 host target gene. DKFZP434L187 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434L187, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L187 BINDING SITE, designated SEQ ID:34127, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44092] Another function of VGAM1231 is therefore inhibition of DKFZP434L187 (Accession XM_044070). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L187. FLJ11004 (Accession NM_018296) is another VGAM1231 host target gene. FLJ11004 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11004 BINDING SITE, designated SEQ ID:20288, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44093] Another function of VGAM1231 is therefore inhibition of FLJ11004 (Accession NM_018296). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ11004. KIAA0495 (Accession XM_031397) is another VGAM1231 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31360, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44094] Another function of VGAM1231 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA1600 (Accession XM_049351) is another VGAM1231 host target gene. KIAA1600 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1600 BINDING SITE, designated SEQ ID:35395, to the

nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44095] Another function of VGAM1231 is therefore inhibition of KIAA1600 (Accession XM_049351). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1600. Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM_015344) is another VGAM1231 host target gene. LEPROTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEPROTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEPROTL1 BINDING SITE, designated SEQ ID:17649, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44096] Another function of VGAM1231 is therefore inhibition of Leptin Receptor Overlapping Transcript-like 1 (LEPROTL1, Accession NM_015344). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEPROTL1. LOC142955 (Accession XM_084389) is another

VGAM1231 host target gene. LOC142955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC142955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142955 BINDING SITE, designated SEQ ID:37570, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44097] Another function of VGAM1231 is therefore inhibition of LOC142955 (Accession XM_084389). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142955. LOC257103 (Accession XM_170982) is another VGAM1231 host target gene. LOC257103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257103 BINDING SITE, designated SEQ ID:45754, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44098] Another function of VGAM1231 is therefore inhibition of LOC257103 (Accession XM_170982). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257103. LOC90148 (Accession XM_029430) is another VGAM1231 host target gene. LOC90148 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90148, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90148 BINDING SITE, designated SEQ ID:30892, to the nucleotide sequence of VGAM1231 RNA, herein designated VGAM RNA, also designated SEQ ID:3942.

[44099] Another function of VGAM1231 is therefore inhibition of LOC90148 (Accession XM_029430). Accordingly, utilities of VGAM1231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90148. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1232 (VGAM1232) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[44100] VGAM1232 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1232 was detected is described hereinabove with reference to Figs. 1–8.

[44101] VGAM1232 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44102] VGAM1232 gene encodes a VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1232 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1232 precursor RNA is designated SEQ ID:1218, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1218 is located at position 14553 relative to the genome of Equine Herpesvirus 2.

[44103] VGAM1232 precursor RNA folds onto itself, forming VGAM1232 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44104] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1232 folded precursor RNA into VGAM1232 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1232 RNA is designated SEQ ID:3943, and is provided hereinbelow with reference to the sequence listing part.

[44105] VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1232 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44106] VGAM1232 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1232 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1232 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44107] The complementary binding of VGAM1232 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1232 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1232 host target RNA into VGAM1232 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44108] It is appreciated that VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1232 host target genes. The mRNA of each one of this plurality of VGAM1232 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1232 RNA, herein designated VGAM RNA, and which when bound by VGAM1232 RNA causes inhibition of translation of respective one or more VGAM1232 host target proteins.

[44109] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1232 gene, herein designated VGAM GENE, on one or more VGAM1232 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44110] It is yet further appreciated that a function of VGAM1232 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1232 correlate with, and may be deduced from, the identity of the host target genes which VGAM1232 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[44111] Nucleotide sequences of the VGAM1232 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1232 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1232 are further described hereinbelow with reference to Table 1.

[44112] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1232 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1232 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44113] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1232 gene, herein designated VGAM is inhibition of expression of VGAM1232 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1232 correlate with, and may be deduced from, the identity of the target genes which VGAM1232 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44114] Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834) is a VGAM1232 host target gene. GRIN2B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GRIN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2B BINDING SITE, designated SEQ ID:6491, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44115] A function of VGAM1232 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN2B. LPTM5 (Accession NM_006762) is another VGAM1232 host target gene. LPTM5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LPTM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPTM5

BINDING SITE, designated SEQ ID:13615, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44116] Another function of VGAM1232 is therefore inhibition of LPTM5 (Accession NM_006762). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPTM5. D15Wsu75e (Accession XM_039495) is another VGAM1232 host target gene. D15Wsu75e BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D15Wsu75e, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D15Wsu75e BINDING SITE, designated SEQ ID:33101, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44117] Another function of VGAM1232 is therefore inhibition of D15Wsu75e (Accession XM_039495). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D15Wsu75e. LOC146452 (Accession XM_085473) is another VGAM1232 host target gene. LOC146452 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146452 BINDING SITE, designated SEQ ID:38161, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44118] Another function of VGAM1232 is therefore inhibition of LOC146452 (Accession XM_085473). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146452. LOC149461 (Accession XM_086547) is another VGAM1232 host target gene. LOC149461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149461 BINDING SITE, designated SEQ ID:38761, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44119] Another function of VGAM1232 is therefore inhibition of

LOC149461 (Accession XM_086547). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149461. LOC222057 (Accession XM_166594) is another VGAM1232 host target gene. LOC222057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222057 BINDING SITE, designated SEQ ID:44573, to the nucleotide sequence of VGAM1232 RNA, herein designated VGAM RNA, also designated SEQ ID:3943.

[44120] Another function of VGAM1232 is therefore inhibition of LOC222057 (Accession XM_166594). Accordingly, utilities of VGAM1232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222057. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1233 (VGAM1233) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[44121] VGAM1233 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1233 was detected is described hereinabove with reference to Figs. 1–8.

[44122] VGAM1233 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44123] VGAM1233 gene encodes a VGAM1233 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1233 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1233 precursor RNA is designated SEQ ID:1219, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1219 is located at position 11297 relative to the genome of Equine Herpesvirus 2.

[44124] VGAM1233 precursor RNA folds onto itself, forming VGAM1233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44125] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1233 folded precursor RNA into VGAM1233 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1233 RNA is designated SEQ ID:3944, and is provided hereinbelow with reference to the sequence listing part.

[44126] VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1233 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44127] VGAM1233 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1233 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1233 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[44128] The complementary binding of VGAM1233 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1233 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1233 host target RNA into VGAM1233 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44129] It is appreciated that VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1233 host target genes. The mRNA of each one of this plurality of VGAM1233 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1233 RNA, herein designated VGAM RNA, and which when bound by VGAM1233 RNA causes inhibition of translation of respective one or more VGAM1233 host target proteins.

[44130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1233 gene, herein designated VGAM GENE, on one

or more VGAM1233 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44131] It is yet further appreciated that a function of VGAM1233 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1233 correlate with, and may be deduced from, the identity of the host target genes which VGAM1233 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44132] Nucleotide sequences of the VGAM1233 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1233 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1233 are further described hereinbelow with reference to Table 1.

[44133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1233 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1233 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44134] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1233 gene, herein designated VGAM is inhibition of expression of VGAM1233 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1233 correlate with, and may be deduced from, the identity of the target genes which VGAM1233 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44135] DNA Fragmentation Factor, 40kDa, Beta Polypeptide

(caspase-activated DNase) (DFFB, Accession XM_113366) is a VGAM1233 host target gene. DFFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DFFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DFFB BINDING SITE, designated SEQ ID:42238, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44136] A function of VGAM1233 is therefore inhibition of DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366), a gene which induces DNA fragmentation and chromatin condensation during apoptosis. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DFFB. The function of DFFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Deiodinase, Iodothyronine, Type III (DIO3, Accession NM_001362) is another VGAM1233 host target gene. DIO3 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by DIO3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO3 BINDING SITE, designated SEQ ID:7041, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44137] Another function of VGAM1233 is therefore inhibition of Deiodinase, Iodothyronine, Type III (DIO3, Accession NM_001362), a gene which regulates circulating fetal thyroid hormone concentrations . Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO3. The function of DIO3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM638.Ectodysplasin 1, Anhidrotic Receptor (EDAR, Accession NM_022336) is another VGAM1233 host target gene. EDAR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EDAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of EDAR BINDING SITE, designated SEQ ID:22744, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44138] Another function of VGAM1233 is therefore inhibition of Ectodysplasin 1, Anhidrotic Receptor (EDAR, Accession NM_022336). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDAR. Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM_000599) is another VGAM1233 host target gene. IGFBP5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IGFBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGFBP5 BINDING SITE, designated SEQ ID:6201, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44139] Another function of VGAM1233 is therefore inhibition of Insulin-like Growth Factor Binding Protein 5 (IGFBP5, Accession NM_000599), a gene which either inhibits or stimulates the growth promoting effects of the igfs on cell culture. Accordingly, utilities of VGAM1233 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with IGFBP5. The function of IGFBP5 has been established by previous studies. See 146733. Allander et al. (1994) cloned the IGFBP5 gene from a human genomic library and showed that it is divided into 4 exons which, primarily due to a first intron of approximately 25 kb, span about 33 kb of DNA. Southern analysis identified a single copy of the IGFBP5 gene in the haploid human genome. By PCR amplification of DNA from somatic human/rodent cell hybrids, by fluorescence in situ hybridization, and by hybridization to pulsed field gel electrophoresis fragments, they showed that the gene is located on 2q33-q34. The IGFBP2 gene (OMIM Ref. No. 146731) and the IGFBP5 gene are transcribed convergently and are separated by approximately 20 to 40 kb of DNA. Primer extension studies identified the IGFBP5 mRNA cap site 772 bp 5-prime to the first nucleotide of the translation start codon. A potential TATA element beginning 33 bp 5-prime to the mRNA cap site was identified. When a DNA fragment containing this cap site and 461 bp of upstream sequence was placed 5-prime to the chloramphenicol acetyltransferase (CAT) reporter gene and transfected into human breast cancer cells, it directed

CAT expression in an orientation-specific manner, suggesting that this region contains elements essential for IGFBP5 promoter activity. Kou et al. (1994) demonstrated that, in the mouse, Igfbp2 and Igfbp5 colocalize to a proximal region of chromosome 1 that is syntenic with human chromosome 2q33-q36 and that the 2 genes are 5 kb apart in a tail-to-tail orientation. This suggests that the human IGFBP5 gene is located on 2q33-q36. Kou et al. (1994) also used interspecific backcross mapping and gene cloning to demonstrate that the Igfbp1 and Igfbp3 are located in the proximal part of chromosome 11. In the human genome, these 2 loci map within 20 kb of one another on 7p14-p12, and the genes are organized in a tail-to-tail configuration. The results suggested to Kou et al. (1994) an evolutionary scheme in which a primordial IGFBP gene duplicated to form a cluster that was later replicated to create a second linkage group.

[44140] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44141] Allander, S. V.; Larsson, C.; Ehrenborg, E.; Suwanichkul, A.; Weber, G.; Morris, S. L.; Bajalica, S.; Kiefer, M. C.; Luthman, H.; Powell, D. R. : Characterization of the chromoso-

mal gene and promoter for human insulin-like growth factor binding protein-5. J. Biol. Chem. 269: 10891-10898, 1994. ; and

[44142] Kou, K.; James, P. L.; Clemmons, D. R.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Rotwein, P. : Identification of two clusters of mouse insulin-like growth factor binding protein.

[44143] Further studies establishing the function and utilities of IGFBP5 are found in John Hopkins OMIM database record ID 146734, and in cited publications numbered 12013 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM_003024) is another VGAM1233 host target gene. ITSN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITSN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITSN1 BINDING SITE, designated SEQ ID:8957, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44144] Another function of VGAM1233 is therefore inhibition of

Intersectin 1 (SH3 domain protein) (ITSN1, Accession NM_003024), a gene which may be involved in endocytosis and synaptic vesicle recycling. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITSN1. The function of ITSN1 has been established by previous studies. See 147265. Ozcelik et al. (1991) found that a cDNA probe for ITPR3 hybridized to DNA from hybrid cells containing human chromosome 6. In one hybrid that carried 6pter-p21, in the absence of an intact copy of this chromosome, hybridization was observed, thus mapping the gene to 6pter-p21. ITPR3 transduces many hormonal signals that regulate Ca^{2+} -dependent processes in the intestinal epithelium. Maranto (1994) described complete sequence of the ITPR3 polypeptide (2,671 amino acids). Primary structure analysis indicated a pattern of conserved and variable regions, characteristic of the particular gene family. Immunocytochemical localization in the intestine was determined. Yamamoto-Hino et al. (1994) likewise mapped the ITPR3 gene to chromosome 6, specifically to 6p21, by isotopic in situ hybridization. They showed that the type 3 receptor was present in all hematopoietic and lymphoma cell lines tested

- [44145] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [44146] Maranto, A. R. : Primary structure, ligand binding, and localization of the human type 3 inositol 1,4,5-trisphosphate receptor expressed in intestinal epithelium. *J. Biol. Chem.* 269: 1222–1230, 1994. ; and
- [44147] Ozcelik, T.; Suedhof, T. C.; Francke, U. : The genes for inositol 1,4,5-trisphosphate receptors 1 (ITPR1) and 3 (ITPR3) are localized on human chromosomes 3p and 6pter–p21, respectively.
- [44148] Further studies establishing the function and utilities of ITSN1 are found in John Hopkins OMIM database record ID 602442, and in cited publications numbered 5612–5613, 586 and 5868 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RNA Binding Motif Protein 3 (RBM3, Accession XM_047024) is another VGAM1233 host target gene. RBM3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RBM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM3 BIND-

ING SITE, designated SEQ ID:34892, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44149] Another function of VGAM1233 is therefore inhibition of RNA Binding Motif Protein 3 (RBM3, Accession XM_047024). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBM3. Regulator of G-protein Signalling 3 (RGS3, Accession NM_017790) is another VGAM1233 host target gene. RGS3 BINDING SITE1 through RGS3 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RGS3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS3 BINDING SITE1 through RGS3 BINDING SITE6, designated SEQ ID:19422, SEQ ID:22086, SEQ ID:29307, SEQ ID:28281, SEQ ID:28667 and SEQ ID:29305 respectively, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44150] Another function of VGAM1233 is therefore inhibition of Regulator of G-protein Signalling 3 (RGS3, Accession

NM_017790), a gene which negatively regulates G protein-coupled receptor signalling. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS3. The function of RGS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404. Transcription Factor Binding to IGHM Enhancer 3 (TFE3, Accession NM_006521) is another VGAM1233 host target gene. TFE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFE3 BINDING SITE, designated SEQ ID:13275, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44151] Another function of VGAM1233 is therefore inhibition of Transcription Factor Binding to IGHM Enhancer 3 (TFE3, Accession NM_006521), a gene which is a positive-acting transcription factor that binds to the immunoglobulin enhancer μ 3 motif. Accordingly, utilities of VGAM1233

include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFE3. The function of TFE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM443. Tumor Suppressing Subtransferable Candidate 4 (TSSC4, Accession NM_005706) is another VGAM1233 host target gene. TSSC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TSSC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSSC4 BINDING SITE, designated SEQ ID:12258, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44152] Another function of VGAM1233 is therefore inhibition of Tumor Suppressing Subtransferable Candidate 4 (TSSC4, Accession NM_005706), a gene which is of unknown function. Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSSC4. The function of TSSC4 has been established by previous studies. Lee et al. (1999)

noted that 7 imprinted genes had been identified on 11p15: IGF2 (OMIM Ref. No. 147470), which encodes an important autocrine growth factor in cancer; H19 (OMIM Ref. No. 103280), an untranslated RNA whose imprinting regulates IGF2; ASCL2 (OMIM Ref. No. 601886), a homolog of *Drosophila* achaete–scute that is expressed in the trophoblast; KCNQ1 (OMIM Ref. No. 192500), which encodes a voltage–gated potassium channel; p57(KIP2) (CDKN1C; 600856), which encodes a cyclin–dependent kinase inhibitor; TSSC5 (IMPT1; 602631), which encodes a predicted transmembrane transporter; and TSSC3 (OMIM Ref. No. 602131), also known as IPL, a homolog of a mouse apoptosis–inducing gene. With the exception of IGF2, all of these genes are expressed from the maternal allele. Because of the large number of imprinted genes on 11p15, spanning approximately 1 Mb, this region appears to represent 1 of 2 known large imprinted domains in the human genome, the other being the Prader–Willi/Angelman syndrome domain of 15q11–q13 (see OMIM Ref. No. 105830). Koi et al. (1993) isolated a sub–chromosomal transferable fragment (STF) that suppresses in vitro growth of the rhabdomyosarcoma cell line RD, confirming the existence of 1 or more tumor suppressor

genes within this region. Hu et al. (1997) found that the STF spans approximately 2.5 Mb, with D11S12 at its proximal end and D11S1318 at its distal end. Within a cluster of imprinted genes in this STF, Lee et al. (1999) identified 2 novel genes, designated TSSC4 and TSSC6 (OMIM Ref. No. 603853), that were not imprinted in any of the fetal or extraembryonic tissues examined. The TSSC4 cDNA encodes a predicted protein of 349 amino acids that shows no close similarity to previously reported proteins. Northern blot analysis revealed that the TSSC4 gene was expressed as an approximately 1.6-kb transcript in fetal brain, lung, liver, and kidney. The TSSC4 and TSSC6 genes are both located in the center of the 1-Mb imprinted domain on 11p15 that contains the 7 imprinted genes. Thus, the imprinted gene domain of 11p15 appears to contain at least 2 imprinted subdomains, between which the TSSC4 and TSSC6 genes substantially escape imprinting, due either to a lack of initial silencing or to an early developmental relaxation of imprinting.

[44153] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44154] Lee, M. P.; Brandenburg, S.; Landes, G. M.; Adams, M.;

Miller, G.; Feinberg, A. P. : Two novel genes in the center of the 11p15 imprinted domain escape genomic imprinting. Hum. Molec. Genet. 8: 683–690, 1999. ; and

[44155] Lee, M. P.; Brandenburg, S.; Landes, G. M.; Adams, M.; Miller, G.; Feinberg, A. P. : Two novel genes in the center of the 11p15 imprinted domain escape genomic imprinting. Hum. Molec. Gene.

[44156] Further studies establishing the function and utilities of TSSC4 are found in John Hopkins OMIM database record ID 603852, and in cited publications numbered 491 and 7419 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726) is another VGAM1233 host target gene. ABCC13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC13 BINDING SITE, designated SEQ ID:28969, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44157] Another function of VGAM1233 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC13. Endothelial Differentiation, Sphingolipid G-protein-coupled Receptor, 1 (EDG1, Accession XM_001499) is another VGAM1233 host target gene. EDG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDG1 BINDING SITE, designated SEQ ID:29841, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44158] Another function of VGAM1233 is therefore inhibition of Endothelial Differentiation, Sphingolipid G-protein-coupled Receptor, 1 (EDG1, Accession XM_001499). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDG1. FLJ12568 (Accession NM_024993) is another VGAM1233 host target gene.

FLJ12568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12568 BINDING SITE, designated SEQ ID:24551, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44159] Another function of VGAM1233 is therefore inhibition of FLJ12568 (Accession NM_024993). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12568. LENG1 (Accession XM_097304) is another VGAM1233 host target gene. LENG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LENG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG1 BINDING SITE, designated SEQ ID:40860, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44160] Another function of VGAM1233 is therefore inhibition of LENG1 (Accession XM_097304). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG1. LIG-1 (Accession XM_033712) is another VGAM1233 host target gene. LIG-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LIG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIG-1 BINDING SITE, designated SEQ ID:31949, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44161] Another function of VGAM1233 is therefore inhibition of LIG-1 (Accession XM_033712). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG-1. MGC10999 (Accession NM_032307) is another VGAM1233 host target gene. MGC10999 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC10999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10999 BINDING SITE, designated SEQ ID:26087, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44162] Another function of VGAM1233 is therefore inhibition of MGC10999 (Accession NM_032307). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10999. MGC2603 (Accession NM_024037) is another VGAM1233 host target gene. MGC2603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2603 BINDING SITE, designated SEQ ID:23470, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44163] Another function of VGAM1233 is therefore inhibition of MGC2603 (Accession NM_024037). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC2603. MGC3113 (Accession NM_024035) is another VGAM1233 host target gene. MGC3113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3113 BINDING SITE, designated SEQ ID:23467, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44164] Another function of VGAM1233 is therefore inhibition of MGC3113 (Accession NM_024035). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3113. SIMRP7 (Accession XM_166462) is another VGAM1233 host target gene. SIMRP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIMRP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIMRP7 BINDING SITE, designated SEQ ID:44367, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA,

also designated SEQ ID:3944.

[44165] Another function of VGAM1233 is therefore inhibition of SIMRP7 (Accession XM_166462). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIMRP7. Testis Specific, 14 (TSGA14, Accession NM_018718) is another VGAM1233 host target gene. TSGA14 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TSGA14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSGA14 BINDING SITE, designated SEQ ID:20792, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44166] Another function of VGAM1233 is therefore inhibition of Testis Specific, 14 (TSGA14, Accession NM_018718). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSGA14. LOC122416 (Accession XM_058615) is another VGAM1233 host target gene. LOC122416 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by

LOC122416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122416 BINDING SITE, designated SEQ ID:36683, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44167] Another function of VGAM1233 is therefore inhibition of LOC122416 (Accession XM_058615). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122416. LOC145439 (Accession XM_085144) is another VGAM1233 host target gene. LOC145439 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145439, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145439 BINDING SITE, designated SEQ ID:37863, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44168] Another function of VGAM1233 is therefore inhibition of LOC145439 (Accession XM_085144). Accordingly, utilities

of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145439. LOC149842 (Accession XM_097745) is another VGAM1233 host target gene. LOC149842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149842 BINDING SITE, designated SEQ ID:41088, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44169] Another function of VGAM1233 is therefore inhibition of LOC149842 (Accession XM_097745). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149842. LOC153338 (Accession XM_098361) is another VGAM1233 host target gene. LOC153338 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153338, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153338 BINDING SITE, designated SEQ ID:41606, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44170] Another function of VGAM1233 is therefore inhibition of LOC153338 (Accession XM_098361). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153338. LOC158654 (Accession XM_088632) is another VGAM1233 host target gene. LOC158654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158654 BINDING SITE, designated SEQ ID:39874, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44171] Another function of VGAM1233 is therefore inhibition of LOC158654 (Accession XM_088632). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158654. LOC162333 (Accession XM_102591) is another VGAM1233 host target gene. LOC162333 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42119, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44172] Another function of VGAM1233 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC254659 (Accession XM_170822) is another VGAM1233 host target gene. LOC254659 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254659 BINDING SITE, designated SEQ ID:45599, to the nucleotide sequence of VGAM1233 RNA, herein designated VGAM RNA, also designated SEQ ID:3944.

[44173] Another function of VGAM1233 is therefore inhibition of

LOC254659 (Accession XM_170822). Accordingly, utilities of VGAM1233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254659. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1234 (VGAM1234) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44174] VGAM1234 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1234 was detected is described hereinabove with reference to Figs. 1-8.

[44175] VGAM1234 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44176] VGAM1234 gene encodes a VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1234 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1234 precursor RNA is designated SEQ ID:1220, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1220 is located at position 11113 relative to the genome of Equine Herpesvirus 2.

- [44177] VGAM1234 precursor RNA folds onto itself, forming VGAM1234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44178] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1234 folded precursor RNA into VGAM1234 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide se-

quence of VGAM1234 RNA is designated SEQ ID:3945, and is provided hereinbelow with reference to the sequence listing part.

[44179] VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1234 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44180] VGAM1234 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1234 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1234 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44181] The complementary binding of VGAM1234 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1234 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1234 host target RNA into VGAM1234 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44182] It is appreciated that VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1234 host target genes. The mRNA of each one of this plurality of VGAM1234 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1234 RNA, herein designated VGAM RNA, and which when bound by VGAM1234 RNA causes inhibition of translation of respective one or more VGAM1234 host target proteins.

[44183] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1234 gene, herein designated VGAM GENE, on one or more VGAM1234 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44184] It is yet further appreciated that a function of VGAM1234

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1234 correlate with, and may be deduced from, the identity of the host target genes which VGAM1234 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44185] Nucleotide sequences of the VGAM1234 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1234 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1234 are further described hereinbelow with reference to Table 1.

[44186] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1234 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1234 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44187] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1234 gene, herein designated VGAM is inhibition of expression of VGAM1234 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1234 correlate with, and may be deduced from, the identity of the target genes which VGAM1234 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44188] Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268) is a VGAM1234 host target gene. REQ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by REQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REQ BINDING SITE, designated SEQ ID:12952, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44189] A function of VGAM1234 is therefore inhibition of Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268), a gene which is a putative zinc finger that is required for apoptosis in murine myeloid cell lines. Accordingly, utilities of VGAM1234 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with REQ. The function of REQ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. CD109 (Accession NM_133493) is another VGAM1234 host target gene. CD109 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD109 BINDING SITE, designated SEQ ID:28570, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44190] Another function of VGAM1234 is therefore inhibition of CD109 (Accession NM_133493). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD109. Ras and Rab Interactor 3 (RIN3, Accession NM_024832) is another VGAM1234 host target gene. RIN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RIN3, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIN3 BINDING SITE, designated SEQ ID:24235, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44191] Another function of VGAM1234 is therefore inhibition of Ras and Rab Interactor 3 (RIN3, Accession NM_024832). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIN3. LOC113655 (Accession NM_138431) is another VGAM1234 host target gene. LOC113655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC113655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113655 BINDING SITE, designated SEQ ID:28795, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44192] Another function of VGAM1234 is therefore inhibition of LOC113655 (Accession NM_138431). Accordingly, utilities

of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113655. LOC145501 (Accession XM_085157) is another VGAM1234 host target gene. LOC145501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145501 BINDING SITE, designated SEQ ID:37882, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44193] Another function of VGAM1234 is therefore inhibition of LOC145501 (Accession XM_085157). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145501. LOC148046 (Accession XM_097375) is another VGAM1234 host target gene. LOC148046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC148046 BINDING SITE, designated SEQ ID:40866, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44194] Another function of VGAM1234 is therefore inhibition of LOC148046 (Accession XM_097375). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148046. LOC196985 (Accession XM_116968) is another VGAM1234 host target gene. LOC196985 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196985, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196985 BINDING SITE, designated SEQ ID:43158, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44195] Another function of VGAM1234 is therefore inhibition of LOC196985 (Accession XM_116968). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196985. LOC89919 (Accession XM_027244) is another VGAM1234 host target gene. LOC89919 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC89919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89919 BINDING SITE, designated SEQ ID:30464, to the nucleotide sequence of VGAM1234 RNA, herein designated VGAM RNA, also designated SEQ ID:3945.

[44196] Another function of VGAM1234 is therefore inhibition of LOC89919 (Accession XM_027244). Accordingly, utilities of VGAM1234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89919. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1235 (VGAM1235) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44197] VGAM1235 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1235 was detected is described hereinabove with reference to Figs. 1-8.

[44198] VGAM1235 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44199] VGAM1235 gene encodes a VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1235 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1235 precursor RNA is designated SEQ ID:1221, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1221 is located at position 102206 relative to the genome of Bovine Herpesvirus 4.

[44200] VGAM1235 precursor RNA folds onto itself, forming VGAM1235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[44201] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1235 folded precursor RNA into VGAM1235 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1235 RNA is designated SEQ ID:3946, and is provided hereinbelow with reference to the sequence listing part.

[44202] VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1235 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44203] VGAM1235 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1235 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1235 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1235 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44204] The complementary binding of VGAM1235 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1235 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1235 host target RNA into VGAM1235 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44205] It is appreciated that VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1235 host target genes. The mRNA of each one of this plurality of VGAM1235 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1235 RNA, herein designated VGAM RNA, and which when bound by VGAM1235 RNA causes inhibition of translation of respective one or more VGAM1235 host target proteins.

[44206] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1235 gene, herein designated VGAM GENE, on one or more VGAM1235 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44207] It is yet further appreciated that a function of VGAM1235 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1235 correlate with, and may be deduced from, the identity of the host target genes which VGAM1235 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44208] Nucleotide sequences of the VGAM1235 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1235 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1235 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1235 are further described hereinbelow with reference to Table 1.

[44209] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1235 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1235 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44210] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1235 gene, herein designated VGAM is inhibition of expression of VGAM1235 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1235 correlate with, and may be deduced from, the identity of the target genes which VGAM1235 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44211] Adducin 2 (beta) (ADD2, Accession NM_017483) is a VGAM1235 host target gene. ADD2 BINDING SITE1 through ADD2 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADD2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of ADD2 BINDING SITE1 through ADD2 BINDING SITE4, designated SEQ ID:18935, SEQ ID:18940, SEQ ID:18943 and SEQ ID:18948 respectively, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44212] A function of VGAM1235 is therefore inhibition of Ad-
ducin 2 (beta) (ADD2, Accession NM_017483), a gene
which membrane-cytoskeleton- protein that promotes the
assembly of the spectrin-actin network. Accordingly, utili-
ties of VGAM1235 include diagnosis, prevention and
treatment of diseases and clinical conditions associated
with ADD2. The function of ADD2 and its association with
various diseases and clinical conditions, has been estab-
lished by previous studies, as described hereinabove with
reference to VGAM1185. Procollagen (type III) N-
endopeptidase (PCOLN3, Accession NM_002768) is an-
other VGAM1235 host target gene. PCOLN3 BINDING SITE
is HOST TARGET binding site found in the 3' untranslated
region of mRNA encoded by PCOLN3, corresponding to a
HOST TARGET binding site such as BINDING SITE I, BIND-
ING SITE II or BINDING SITE III. Table 2 illustrates the com-
plementarity of the nucleotide sequences of PCOLN3

BINDING SITE, designated SEQ ID:8662, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44213] Another function of VGAM1235 is therefore inhibition of Procollagen (type III) N-endopeptidase (PCOLN3, Accession NM_002768), a gene which is a member of the zincin superfamily of zinc-dependent metalloproteases. Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCOLN3. The function of PCOLN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM947. Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600) is another VGAM1235 host target gene. TCF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF3 BINDING SITE, designated SEQ ID:35009, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ

ID:3946.

[44214] Another function of VGAM1235 is therefore inhibition of Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600), a gene which plays major roles in determining tissue-specific cell fate during embryogenesis. Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF3. The function of TCF3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. DKFZp547I224 (Accession NM_020221) is another VGAM1235 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21473, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44215] Another function of VGAM1235 is therefore inhibition of

DKFZp547I224 (Accession NM_020221). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I224. Fidgetin (FIGN, Accession NM_018086) is another VGAM1235 host target gene. FIGN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FIGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FIGN BINDING SITE, designated SEQ ID:19848, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44216] Another function of VGAM1235 is therefore inhibition of Fidgetin (FIGN, Accession NM_018086). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FIGN. FLJ12891 (Accession NM_024950) is another VGAM1235 host target gene. FLJ12891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ12891 BINDING SITE, designated SEQ ID:24510, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44217] Another function of VGAM1235 is therefore inhibition of FLJ12891 (Accession NM_024950). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12891. FLJ22865 (Accession NM_025109) is another VGAM1235 host target gene. FLJ22865 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22865 BINDING SITE, designated SEQ ID:24758, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44218] Another function of VGAM1235 is therefore inhibition of FLJ22865 (Accession NM_025109). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22865. KIAA0295 (Accession XM_042833) is another

VGAM1235 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33782, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44219] Another function of VGAM1235 is therefore inhibition of KIAA0295 (Accession XM_042833). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. KIAA1280 (Accession XM_045766) is another VGAM1235 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34554, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44220] Another function of VGAM1235 is therefore inhibition of KIAA1280 (Accession XM_045766). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1987 (Accession XM_113870) is another VGAM1235 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42493, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44221] Another function of VGAM1235 is therefore inhibition of KIAA1987 (Accession XM_113870). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1235 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12794, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44222] Another function of VGAM1235 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM_170929) is another VGAM1235 host target gene. PDE4DIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4DIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4DIP BINDING SITE, designated SEQ ID:45708, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44223] Another function of VGAM1235 is therefore inhibition of

Phosphodiesterase 4D Interacting Protein (myomegalin) (PDE4DIP, Accession XM_170929). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4DIP. PRO1496 (Accession NM_018603) is another VGAM1235 host target gene. PRO1496 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1496 BINDING SITE, designated SEQ ID:20680, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44224] Another function of VGAM1235 is therefore inhibition of PRO1496 (Accession NM_018603). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1496. LOC219920 (Accession XM_167787) is another VGAM1235 host target gene. LOC219920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219920, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219920 BINDING SITE, designated SEQ ID:44807, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44225] Another function of VGAM1235 is therefore inhibition of LOC219920 (Accession XM_167787). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219920. LOC92568 (Accession XM_045852) is another VGAM1235 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34578, to the nucleotide sequence of VGAM1235 RNA, herein designated VGAM RNA, also designated SEQ ID:3946.

[44226] Another function of VGAM1235 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM1235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92568. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1236 (VGAM1236) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44227] VGAM1236 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1236 was detected is described hereinabove with reference to Figs. 1–8.

[44228] VGAM1236 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44229] VGAM1236 gene encodes a VGAM1236 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1236 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1236 precursor RNA is designated SEQ ID:1222, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1222 is located at position 104518 relative to the genome of Bovine Herpesvirus 4.

- [44230] VGAM1236 precursor RNA folds onto itself, forming VGAM1236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44231] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1236 folded precursor RNA into VGAM1236 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1236 RNA is designated SEQ ID:3947, and is provided hereinbelow with reference to the sequence listing part.

[44232] VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1236 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44233] VGAM1236 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1236 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1236 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44234] The complementary binding of VGAM1236 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1236 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1236 host target RNA into VGAM1236 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44235] It is appreciated that VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1236 host target genes. The mRNA of each one of this plurality of VGAM1236 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1236 RNA, herein designated VGAM RNA, and which when bound by VGAM1236 RNA causes

inhibition of translation of respective one or more VGAM1236 host target proteins.

[44236] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1236 gene, herein designated VGAM GENE, on one or more VGAM1236 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44237] It is yet further appreciated that a function of VGAM1236 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1236 include diagnosis, prevention and

treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1236 correlate with, and may be deduced from, the identity of the host target genes which VGAM1236 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44238] Nucleotide sequences of the VGAM1236 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1236 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1236 are further described hereinbelow with reference to Table 1.

[44239] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1236 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1236 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44240] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1236 gene, herein designated VGAM is inhibition of expression of VGAM1236 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1236 correlate with, and may be deduced from, the identity of the target genes which VGAM1236 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44241] Sex Comb On Midleg-like 2 (Drosophila) (SCML2, Accession NM_006089) is a VGAM1236 host target gene. SCML2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCML2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCML2 BINDING SITE, designated SEQ ID:12735, to the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, also designated SEQ ID:3947.

[44242] A function of VGAM1236 is therefore inhibition of Sex Comb On Midleg-like 2 (Drosophila) (SCML2, Accession NM_006089). Accordingly, utilities of VGAM1236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCML2. TRAM (Accession NM_014294) is another VGAM1236 host target gene. TRAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAM,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAM BINDING SITE, designated SEQ ID:15591, to the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, also designated SEQ ID:3947.

[44243] Another function of VGAM1236 is therefore inhibition of TRAM (Accession NM_014294). Accordingly, utilities of VGAM1236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAM. KIAA0831 (Accession NM_014924) is another VGAM1236 host target gene. KIAA0831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0831 BINDING SITE, designated SEQ ID:17206, to the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, also designated SEQ ID:3947.

[44244] Another function of VGAM1236 is therefore inhibition of KIAA0831 (Accession NM_014924). Accordingly, utilities of VGAM1236 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0831. KIAA1300 (Accession XM_031744) is another VGAM1236 host target gene. KIAA1300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1300 BINDING SITE, designated SEQ ID:31480, to the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, also designated SEQ ID:3947.

[44245] Another function of VGAM1236 is therefore inhibition of KIAA1300 (Accession XM_031744). Accordingly, utilities of VGAM1236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1300. LOC130813 (Accession XM_065904) is another VGAM1236 host target gene. LOC130813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130813 BINDING SITE, designated SEQ ID:37306, to

the nucleotide sequence of VGAM1236 RNA, herein designated VGAM RNA, also designated SEQ ID:3947.

[44246] Another function of VGAM1236 is therefore inhibition of LOC130813 (Accession XM_065904). Accordingly, utilities of VGAM1236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1237 (VGAM1237) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44247] VGAM1237 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1237 was detected is described hereinabove with reference to Figs. 1–8.

[44248] VGAM1237 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44249] VGAM1237 gene encodes a VGAM1237 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1237 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1237 precursor RNA is designated SEQ ID:1223, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1223 is located at position 100957 relative to the genome of Bovine Herpesvirus 4.

[44250] VGAM1237 precursor RNA folds onto itself, forming VGAM1237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44251] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1237 folded precursor RNA into VGAM1237 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1237 RNA is designated SEQ ID:3948, and is provided hereinbelow with reference to the sequence listing part.

[44252] VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1237 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44253] VGAM1237 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1237 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1237 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44254] The complementary binding of VGAM1237 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1237 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1237 host target RNA into VGAM1237 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44255] It is appreciated that VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1237 host target genes. The mRNA of each one of this plurality of VGAM1237 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1237 RNA, herein designated VGAM RNA, and which when bound by VGAM1237 RNA causes inhibition of translation of respective one or more VGAM1237 host target proteins.

[44256] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1237 gene, herein designated VGAM GENE, on one or more VGAM1237 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[44257] It is yet further appreciated that a function of VGAM1237 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1237 correlate with, and may be deduced from, the identity of the host target genes which VGAM1237 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44258] Nucleotide sequences of the VGAM1237 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1237 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1237 are further described hereinbelow with reference to Table 1.

[44259] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1237 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1237 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44260] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1237 gene, herein designated VGAM is inhibition of expression of VGAM1237 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1237 correlate with, and may be deduced from, the identity of the target genes which VGAM1237 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44261] Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093) is a VGAM1237 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11551, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44262] A function of VGAM1237 is therefore inhibition of Core-

binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. RAB5B, Member RAS Oncogene Family (RAB5B, Accession NM_002868) is another VGAM1237 host target gene. RAB5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB5B BINDING SITE, designated SEQ ID:8773, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44263] Another function of VGAM1237 is therefore inhibition of RAB5B, Member RAS Oncogene Family (RAB5B, Accession NM_002868), a gene which is presumably involved in vesicular trafficking at the plasma membrane. Accord-

ingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB5B. The function of RAB5B has been established by previous studies. A number of processes in eukaryotic cells are believed to be regulated by small, monomeric GTPases belonging to the RAS superfamily. A subset of these GTPases (the yeast YPT1/SEC4 gene products and their mammalian counterparts, the RAB proteins) plays a central role in membrane trafficking. Each of the several proteins of this subfamily that have been identified is thought to regulate vesicular trafficking at a specific subcellular compartment. The subcellular location of several RAB proteins has been determined by immunohistochemical methods. For example, RAB2 (OMIM Ref. No. 179509) is found in the intermediate recycling pathway between the endoplasmic reticulum and the Golgi complex. RAB6 (OMIM Ref. No. 179513) is distributed in the medial and trans Golgi. RAB4 (OMIM Ref. No. 179511) and RAB5A (OMIM Ref. No. 179512) are associated with the plasma membrane and early endosomes. Wilson and Wilson (1992) cloned cDNA of a novel member of the RAB family by screening a human umbilical vein endothelial cell cDNA library with oligonucleotide probes correspond-

ing to a region conserved in all RAB proteins. The newly identified RAB protein was 81% identical to human RAB5, the canine counterpart of which had been localized to the plasma membrane and early endosomes. In light of this homology, Wilson and Wilson (1992) called the new member of the GTPase superfamily RAB5B. It is presumably involved in vesicular trafficking at the plasma membrane. By fluorescence in situ hybridization, Korenberg et al. (1995) mapped the RAB5B gene to 12q13.

[44264] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44265] Korenberg, J. R.; Chen, X.-N.; Adams, M. D.; Venter, J. C. : Toward a cDNA map of the human genome. *Genomics* 29: 364–370, 1995. ; and

[44266] Wilson, D. B.; Wilson, M. P. : Identification and subcellular localization of human rab5b, a new member of the ras-related superfamily of GTPases. *J. Clin. Invest.* 89: 996–1005, 1992.

[44267] Further studies establishing the function and utilities of RAB5B are found in John Hopkins OMIM database record ID 179514, and in cited publications numbered 2545–2546 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM_015385) is another VGAM1237 host target gene. SORBS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SORBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SORBS1 BINDING SITE, designated SEQ ID:17688, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44268] Another function of VGAM1237 is therefore inhibition of Sorbin and SH3 Domain Containing 1 (SORBS1, Accession NM_015385), a gene which necessary for cell polarization during vegetative growth. Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SORBS1. The function of SORBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475. Chromosome 20 Open Reading Frame 18 (C20orf18, Accession NM_031228) is another

VGAM1237 host target gene. C20orf18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf18 BINDING SITE, designated SEQ ID:25274, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44269] Another function of VGAM1237 is therefore inhibition of Chromosome 20 Open Reading Frame 18 (C20orf18, Accession NM_031228). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf18. Chromosome 20 Open Reading Frame 30 (C20orf30, Accession NM_014145) is another VGAM1237 host target gene. C20orf30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf30 BINDING SITE, designated SEQ ID:15430, to the nucleotide sequence of VGAM1237 RNA,

herein designated VGAM RNA, also designated SEQ ID:3948.

[44270] Another function of VGAM1237 is therefore inhibition of Chromosome 20 Open Reading Frame 30 (C20orf30, Accession NM_014145). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf30.

FLJ13612 (Accession NM_025202) is another VGAM1237 host target gene. FLJ13612 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13612 BINDING SITE, designated SEQ ID:24864, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44271] Another function of VGAM1237 is therefore inhibition of FLJ13612 (Accession NM_025202). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13612. Growth Hormone Inducible Transmembrane Protein (GHITM, Accession NM_014394) is another

VGAM1237 host target gene. GHITM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHITM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GHITM BINDING SITE, designated SEQ ID:15726, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44272] Another function of VGAM1237 is therefore inhibition of Growth Hormone Inducible Transmembrane Protein (GHITM, Accession NM_014394). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHITM. KIAA0700 (Accession XM_050561) is another VGAM1237 host target gene. KIAA0700 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0700 BINDING SITE, designated SEQ ID:35660, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3948.

[44273] Another function of VGAM1237 is therefore inhibition of KIAA0700 (Accession XM_050561). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0700. KIAA1877 (Accession XM_038616) is another VGAM1237 host target gene. KIAA1877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1877 BINDING SITE, designated SEQ ID:32884, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44274] Another function of VGAM1237 is therefore inhibition of KIAA1877 (Accession XM_038616). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1877. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737) is another VGAM1237 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by RASSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16394, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44275] Another function of VGAM1237 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. SPEC1 (Accession NM_020239) is another VGAM1237 host target gene. SPEC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPEC1 BINDING SITE, designated SEQ ID:21512, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44276] Another function of VGAM1237 is therefore inhibition of

SPEC1 (Accession NM_020239). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPEC1. LOC143425 (Accession XM_113695) is another VGAM1237 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143425 BINDING SITE, designated SEQ ID:42348, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44277] Another function of VGAM1237 is therefore inhibition of LOC143425 (Accession XM_113695). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC149832 (Accession XM_097733) is another VGAM1237 host target gene. LOC149832 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149832 BINDING SITE, designated SEQ ID:41082, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44278] Another function of VGAM1237 is therefore inhibition of LOC149832 (Accession XM_097733). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149832. LOC150319 (Accession XM_086816) is another VGAM1237 host target gene. LOC150319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150319 BINDING SITE, designated SEQ ID:38895, to the nucleotide sequence of VGAM1237 RNA, herein designated VGAM RNA, also designated SEQ ID:3948.

[44279] Another function of VGAM1237 is therefore inhibition of LOC150319 (Accession XM_086816). Accordingly, utilities of VGAM1237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150319. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1238 (VGAM1238) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44280] VGAM1238 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1238 was detected is described hereinabove with reference to Figs. 1–8.

[44281] VGAM1238 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44282] VGAM1238 gene encodes a VGAM1238 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1238 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1238 precursor RNA is designated SEQ ID:1224, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1224 is located at position 105956 relative to the genome of Bovine Herpesvirus 4.

[44283] VGAM1238 precursor RNA folds onto itself, forming VGAM1238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44284] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1238 folded precursor RNA into VGAM1238 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1238 RNA is designated SEQ ID:3949, and is provided hereinbelow with reference to the sequence listing part.

[44285] VGAM1238 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1238 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44286] VGAM1238 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1238 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1238 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1238 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[44287] The complementary binding of VGAM1238 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1238 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1238 host target RNA into VGAM1238 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44288] It is appreciated that VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1238 host target genes. The mRNA of each one of this plurality of VGAM1238 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1238 RNA, herein designated VGAM RNA, and which when bound by VGAM1238 RNA causes inhibition of translation of respective one or more

VGAM1238 host target proteins.

[44289] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1238 gene, herein designated VGAM GENE, on one or more VGAM1238 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44290] It is yet further appreciated that a function of VGAM1238 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM1238 correlate with, and may be deduced from, the identity of the host target genes which VGAM1238 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44291] Nucleotide sequences of the VGAM1238 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1238 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1238 are further described hereinbelow with reference to Table 1.

[44292] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1238 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1238 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44293] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1238 gene, herein designated VGAM is inhibition of expression of VGAM1238 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1238 correlate with, and may be deduced from, the identity of the target genes which VGAM1238 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44294] AXIN1 Up-regulated 1 (AXUD1, Accession NM_033027) is a VGAM1238 host target gene. AXUD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AXUD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXUD1 BINDING SITE, designated SEQ ID:26916, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44295] A function of VGAM1238 is therefore inhibition of AXIN1 Up-regulated 1 (AXUD1, Accession NM_033027). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXUD1. Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM_006030) is another VGAM1238 host target gene. CACNA2D2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CACNA2D2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA2D2 BINDING SITE, designated SEQ ID:12647, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44296] Another function of VGAM1238 is therefore inhibition of Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM_006030), a gene which is a calcium channel protein which plays an important role in excitation-contraction coupling. Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA2D2. The function of CACNA2D2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM203. Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502) is another VGAM1238 host target gene. CX3CR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CX3CR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CX3CR1 BINDING SITE, designated SEQ ID:34977, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44297] Another function of VGAM1238 is therefore inhibition of Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502), a gene which mediates both the adhesive and migratory functions of fractalkine. Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CX3CR1. The function of CX3CR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Peroxisome Biogenesis Factor 10 (PEX10, Accession NM_002617) is another VGAM1238 host target gene. PEX10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEX10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX10 BINDING SITE, designated SEQ ID:8478, to the nucleotide sequence of

VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44298] Another function of VGAM1238 is therefore inhibition of Peroxisome Biogenesis Factor 10 (PEX10, Accession NM_002617). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX10. Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM_042096) is another VGAM1238 host target gene. RRM2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRM2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRM2B BINDING SITE, designated SEQ ID:33687, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44299] Another function of VGAM1238 is therefore inhibition of Ribonucleotide Reductase M2 B (TP53 inducible) (RRM2B, Accession XM_042096). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRM2B.

Tumor-associated Calcium Signal Transducer 2 (TACSTD2, Accession NM_002353) is another VGAM1238 host target gene. TACSTD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TACSTD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TACSTD2 BINDING SITE, designated SEQ ID:8157, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44300] Another function of VGAM1238 is therefore inhibition of Tumor-associated Calcium Signal Transducer 2 (TACSTD2, Accession NM_002353), a gene which belongs to ga733 tumor-associated antigen gene family and may function as growth factor receptors. Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACSTD2. The function of TACSTD2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210.DKFZP564D116 (Accession XM_051050) is another VGAM1238 host target gene. DK-

FZP564D116 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D116 BINDING SITE, designated SEQ ID:35733, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44301] Another function of VGAM1238 is therefore inhibition of DKFZP564D116 (Accession XM_051050). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D116. FLJ14855 (Accession NM_033210) is another VGAM1238 host target gene. FLJ14855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14855 BINDING SITE, designated SEQ ID:27057, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44302] Another function of VGAM1238 is therefore inhibition of FLJ14855 (Accession NM_033210). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14855. FLJ21709 (Accession XM_085480) is another VGAM1238 host target gene. FLJ21709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21709 BINDING SITE, designated SEQ ID:38166, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44303] Another function of VGAM1238 is therefore inhibition of FLJ21709 (Accession XM_085480). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21709. FLJ22477 (Accession NM_024735) is another VGAM1238 host target gene. FLJ22477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22477 BINDING SITE, designated SEQ ID:24074, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44304] Another function of VGAM1238 is therefore inhibition of FLJ22477 (Accession NM_024735). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22477. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044) is another VGAM1238 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:17396 and SEQ ID:28916 respectively, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44305] Another function of VGAM1238 is therefore inhibition of

Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. MGC16075 (Accession NM_032761) is another VGAM1238 host target gene. MGC16075 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16075, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16075 BINDING SITE, designated SEQ ID:26503, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44306] Another function of VGAM1238 is therefore inhibition of MGC16075 (Accession NM_032761). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16075. POPX1 (Accession NM_014906) is another VGAM1238 host target gene. POPX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POPX1 BINDING SITE, designated SEQ ID:17115, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44307] Another function of VGAM1238 is therefore inhibition of POPX1 (Accession NM_014906). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POPX1. RALGPS1A (Accession NM_014636) is another VGAM1238 host target gene. RALGPS1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALGPS1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALGPS1A BINDING SITE, designated SEQ ID:16013, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44308] Another function of VGAM1238 is therefore inhibition of RALGPS1A (Accession NM_014636). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

RALGPS1A. RSP3 (Accession NM_031924) is another VGAM1238 host target gene. RSP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RSP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RSP3 BINDING SITE, designated SEQ ID:25671, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44309] Another function of VGAM1238 is therefore inhibition of RSP3 (Accession NM_031924). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RSP3. LOC138399 (Accession XM_059971) is another VGAM1238 host target gene. LOC138399 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138399 BINDING SITE, designated SEQ ID:37129, to the nucleotide sequence of VGAM1238 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3949.

[44310] Another function of VGAM1238 is therefore inhibition of LOC138399 (Accession XM_059971). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138399. LOC139231 (Accession XM_060020) is another VGAM1238 host target gene. LOC139231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139231 BINDING SITE, designated SEQ ID:37141, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44311] Another function of VGAM1238 is therefore inhibition of LOC139231 (Accession XM_060020). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139231. LOC149706 (Accession XM_097718) is another VGAM1238 host target gene. LOC149706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149706, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149706 BINDING SITE, designated SEQ ID:41056, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44312] Another function of VGAM1238 is therefore inhibition of LOC149706 (Accession XM_097718). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149706. LOC150282 (Accession XM_086852) is another VGAM1238 host target gene. LOC150282 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150282, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150282 BINDING SITE, designated SEQ ID:38918, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44313] Another function of VGAM1238 is therefore inhibition of LOC150282 (Accession XM_086852). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150282. LOC221474 (Accession XM_166464) is another VGAM1238 host target gene. LOC221474 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC221474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221474 BINDING SITE, designated SEQ ID:44376, to the nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44314] Another function of VGAM1238 is therefore inhibition of LOC221474 (Accession XM_166464). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221474. LOC93589 (Accession XM_052387) is another VGAM1238 host target gene. LOC93589 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC93589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93589 BINDING SITE, designated SEQ ID:35974, to the

nucleotide sequence of VGAM1238 RNA, herein designated VGAM RNA, also designated SEQ ID:3949.

[44315] Another function of VGAM1238 is therefore inhibition of LOC93589 (Accession XM_052387). Accordingly, utilities of VGAM1238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93589. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1239 (VGAM1239) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44316] VGAM1239 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1239 was detected is described hereinabove with reference to Figs. 1–8.

[44317] VGAM1239 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44318] VGAM1239 gene encodes a VGAM1239 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1239 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1239 precursor RNA is designated SEQ ID:1225, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1225 is located at position 106225 relative to the genome of Bovine Herpesvirus 4.

[44319] VGAM1239 precursor RNA folds onto itself, forming VGAM1239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44320] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1239 folded precursor RNA into VGAM1239 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1239 RNA is designated SEQ ID:3950, and is provided hereinbelow with reference to the sequence listing part.

[44321] VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1239 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44322] VGAM1239 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1239 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1239 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44323] The complementary binding of VGAM1239 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1239 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1239 host target RNA into VGAM1239 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44324] It is appreciated that VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1239 host target genes. The mRNA of each one of this plurality of VGAM1239 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1239 RNA, herein designated VGAM RNA, and which when bound by VGAM1239 RNA causes inhibition of translation of respective one or more VGAM1239 host target proteins.

[44325] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1239 gene, herein designated VGAM GENE, on one or more VGAM1239 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[44326] It is yet further appreciated that a function of VGAM1239 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1239 correlate with, and may be deduced from, the identity of the host target genes which VGAM1239 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44327] Nucleotide sequences of the VGAM1239 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1239 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1239 are further described hereinbelow with reference to Table 1.

[44328] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1239 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1239 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44329] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1239 gene, herein designated VGAM is inhibition of expression of VGAM1239 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1239 correlate with, and may be deduced from, the identity of the target genes which VGAM1239 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44330] Collagen, Type III, Alpha 1 (Ehlers–Danlos syndrome type IV, autosomal dominant) (COL3A1, Accession NM_000090) is a VGAM1239 host target gene. COL3A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COL3A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL3A1 BINDING SITE, designated SEQ ID:5543, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44331] A function of VGAM1239 is therefore inhibition of Colla–

gen, Type III, Alpha 1 (Ehlers–Danlos syndrome type IV, autosomal dominant) (COL3A1, Accession NM_000090). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL3A1. CXYorf1 (Accession XM_088704) is another VGAM1239 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39903, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44332] Another function of VGAM1239 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. TRIP–Br2 (Accession NM_014755) is another VGAM1239 host target gene. TRIP–Br2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIP–Br2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16490, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44333] Another function of VGAM1239 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. LOC199725 (Accession XM_117119) is another VGAM1239 host target gene. LOC199725 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199725 BINDING SITE, designated SEQ ID:43241, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44334] Another function of VGAM1239 is therefore inhibition of LOC199725 (Accession XM_117119). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC199725. LOC200093 (Accession XM_032184) is another VGAM1239 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31595, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44335] Another function of VGAM1239 is therefore inhibition of LOC200093 (Accession XM_032184). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC91040 (Accession XM_035641) is another VGAM1239 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32312, to the

nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44336] Another function of VGAM1239 is therefore inhibition of LOC91040 (Accession XM_035641). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. LOC91464 (Accession XM_038589) is another VGAM1239 host target gene. LOC91464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91464 BINDING SITE, designated SEQ ID:32873, to the nucleotide sequence of VGAM1239 RNA, herein designated VGAM RNA, also designated SEQ ID:3950.

[44337] Another function of VGAM1239 is therefore inhibition of LOC91464 (Accession XM_038589). Accordingly, utilities of VGAM1239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1240 (VGAM1240) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44338] VGAM1240 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1240 was detected is described hereinabove with reference to Figs. 1–8.

[44339] VGAM1240 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 4. VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44340] VGAM1240 gene encodes a VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1240 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1240 precursor RNA is designated SEQ ID:1226, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1226 is located at position 100575 relative to the genome of Bovine Herpesvirus 4.

[44341] VGAM1240 precursor RNA folds onto itself, forming VGAM1240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44342] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1240 folded precursor RNA into VGAM1240 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM1240 RNA is designated SEQ ID:3951, and is provided hereinbelow with reference to the sequence listing part.

[44343] VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1240 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1240 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44344] VGAM1240 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1240 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1240 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44345] The complementary binding of VGAM1240 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1240 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1240 host target RNA into VGAM1240 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44346] It is appreciated that VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1240 host target genes. The mRNA of each one of this plurality of VGAM1240 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1240 RNA, herein designated VGAM RNA, and which when bound by VGAM1240 RNA causes inhibition of translation of respective one or more VGAM1240 host target proteins.

[44347] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1240 gene, herein designated VGAM GENE, on one or more VGAM1240 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44348] It is yet further appreciated that a function of VGAM1240 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM1240 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1240 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44349] Nucleotide sequences of the VGAM1240 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1240 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1240 are further described hereinbelow with reference to Table 1.

[44350] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1240 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1240 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44351] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1240 gene, herein designated VGAM is inhibition of expression of VGAM1240 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1240 correlate with, and may be deduced from, the identity of the target genes which VGAM1240

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44352] Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862) is a VGAM1240 host target gene. ARNT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNT2 BINDING SITE, designated SEQ ID:16931, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44353] A function of VGAM1240 is therefore inhibition of Aryl–hydrocarbon Receptor Nuclear Translocator 2 (ARNT2, Accession NM_014862), a gene which specifically recognizes the xenobiotic response element (xre). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNT2. The function of ARNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM345. Arginine Vasopressin Recep–

tor 1A (AVPR1A, Accession NM_000706) is another VGAM1240 host target gene. AVPR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AVPR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AVPR1A BINDING SITE, designated SEQ ID:6377, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44354] Another function of VGAM1240 is therefore inhibition of Arginine Vasopressin Receptor 1A (AVPR1A, Accession NM_000706), a gene which mediates cell contraction and proliferation, platelet aggregation, release of coagulation factor, and glycogenolysis. Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AVPR1A. The function of AVPR1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM549. Kelch-like 2, Mayven (*Drosophila*) (KLHL2, Accession NM_007246) is another VGAM1240 host target gene. KLHL2 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KLHL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL2 BINDING SITE, designated SEQ ID:14113, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44355] Another function of VGAM1240 is therefore inhibition of Kelch-like 2, Mayven (Drosophila) (KLHL2, Accession NM_007246). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL2. Mannose Receptor, C Type 1 (MRC1, Accession NM_002438) is another VGAM1240 host target gene. MRC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRC1 BINDING SITE, designated SEQ ID:8280, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44356] Another function of VGAM1240 is therefore inhibition of Mannose Receptor, C Type 1 (MRC1, Accession NM_002438), a gene which mediates the endocytosis of glycoproteins. Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRC1. The function of MRC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1217. Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM_002474) is another VGAM1240 host target gene. MYH11 BINDING SITE1 and MYH11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MYH11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH11 BINDING SITE1 and MYH11 BINDING SITE2, designated SEQ ID:8303 and SEQ ID:23145 respectively, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44357] Another function of VGAM1240 is therefore inhibition of Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11,

Accession NM_002474), a gene which is involved in muscle contraction. Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH11. The function of MYH11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.CG018 (Accession NM_052818) is another VGAM1240 host target gene. CG018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CG018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG018 BINDING SITE, designated SEQ ID:27402, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44358] Another function of VGAM1240 is therefore inhibition of CG018 (Accession NM_052818). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG018. DKFZP434B172 (Accession XM_046264) is another VGAM1240 host target gene. DKFZP434B172 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434B172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B172 BINDING SITE, designated SEQ ID:34701, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44359] Another function of VGAM1240 is therefore inhibition of DKFZP434B172 (Accession XM_046264). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B172. DKFZP564M182 (Accession XM_085525) is another VGAM1240 host target gene. DKFZP564M182 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564M182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564M182 BINDING SITE, designated SEQ ID:38217, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3951.

[44360] Another function of VGAM1240 is therefore inhibition of DKFZP564M182 (Accession XM_085525). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564M182. FLJ10830 (Accession NM_018235) is another VGAM1240 host target gene. FLJ10830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10830 BINDING SITE, designated SEQ ID:20185, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44361] Another function of VGAM1240 is therefore inhibition of FLJ10830 (Accession NM_018235). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10830. FLJ12572 (Accession NM_022905) is another VGAM1240 host target gene. FLJ12572 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12572, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23200, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44362] Another function of VGAM1240 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. FLJ12592 (Accession NM_032169) is another VGAM1240 host target gene. FLJ12592 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12592, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12592 BINDING SITE, designated SEQ ID:25877, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44363] Another function of VGAM1240 is therefore inhibition of FLJ12592 (Accession NM_032169). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12592. HSPC043 (Accession XM_041943) is another VGAM1240 host target gene. HSPC043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC043 BINDING SITE, designated SEQ ID:33638, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44364] Another function of VGAM1240 is therefore inhibition of HSPC043 (Accession XM_041943). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC043. KIAA0052 (Accession XM_042108) is another VGAM1240 host target gene. KIAA0052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0052 BINDING SITE, designated SEQ ID:33693, to the

nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44365] Another function of VGAM1240 is therefore inhibition of KIAA0052 (Accession XM_042108). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0052. KIAA0532 (Accession XM_047659) is another VGAM1240 host target gene. KIAA0532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0532 BINDING SITE, designated SEQ ID:35020, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44366] Another function of VGAM1240 is therefore inhibition of KIAA0532 (Accession XM_047659). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0532. KIAA1719 (Accession XM_042936) is another VGAM1240 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33823, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44367] Another function of VGAM1240 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277) is another VGAM1240 host target gene. KLK7 BINDING SITE1 and KLK7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK7 BINDING SITE1 and KLK7 BINDING SITE2, designated SEQ ID:29276 and SEQ ID:11479 respectively, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44368] Another function of VGAM1240 is therefore inhibition of Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK7. MGC27382 (Accession NM_144700) is another VGAM1240 host target gene. MGC27382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC27382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC27382 BINDING SITE, designated SEQ ID:29522, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44369] Another function of VGAM1240 is therefore inhibition of MGC27382 (Accession NM_144700). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC27382. MISS (Accession NM_144578) is another VGAM1240 host target gene. MISS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MISS, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MISS BINDING SITE, designated SEQ ID:29383, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44370] Another function of VGAM1240 is therefore inhibition of MISS (Accession NM_144578). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MISS. Neurolysin (metallopeptidase M3 family) (NLN, Accession NM_020726) is another VGAM1240 host target gene. NLN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NLN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NLN BINDING SITE, designated SEQ ID:21858, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44371] Another function of VGAM1240 is therefore inhibition of Neurolysin (metallopeptidase M3 family) (NLN, Accession NM_020726). Accordingly, utilities of VGAM1240 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NLN. PRO0097 (Accession NM_014114) is another VGAM1240 host target gene. PRO0097 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO0097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0097 BINDING SITE, designated SEQ ID:15362, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44372] Another function of VGAM1240 is therefore inhibition of PRO0097 (Accession NM_014114). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0097. RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM_032918) is another VGAM1240 host target gene. RERG BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RERG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of RERG BINDING SITE, designated SEQ ID:26736, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44373] Another function of VGAM1240 is therefore inhibition of RAS-like, Estrogen-regulated, Growth-inhibitor (RERG, Accession NM_032918). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERG. LOC123435 (Accession XM_058706) is another VGAM1240 host target gene. LOC123435 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123435 BINDING SITE, designated SEQ ID:36724, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44374] Another function of VGAM1240 is therefore inhibition of LOC123435 (Accession XM_058706). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC123435. LOC147837 (Accession XM_085915) is another VGAM1240 host target gene. LOC147837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147837 BINDING SITE, designated SEQ ID:38394, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44375] Another function of VGAM1240 is therefore inhibition of LOC147837 (Accession XM_085915). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147837. LOC153894 (Accession XM_087796) is another VGAM1240 host target gene. LOC153894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153894 BINDING SITE, designated SEQ ID:39428, to the nucleotide sequence of VGAM1240 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3951.

[44376] Another function of VGAM1240 is therefore inhibition of LOC153894 (Accession XM_087796). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153894. LOC154442 (Accession XM_098536) is another VGAM1240 host target gene. LOC154442 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154442 BINDING SITE, designated SEQ ID:41707, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44377] Another function of VGAM1240 is therefore inhibition of LOC154442 (Accession XM_098536). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154442. LOC255328 (Accession XM_172920) is another VGAM1240 host target gene. LOC255328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255328, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255328 BINDING SITE, designated SEQ ID:46177, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44378] Another function of VGAM1240 is therefore inhibition of LOC255328 (Accession XM_172920). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255328. LOC51696 (Accession NM_016217) is another VGAM1240 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18305, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44379] Another function of VGAM1240 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC51696. LOC91012 (Accession XM_035503) is another VGAM1240 host target gene. LOC91012 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91012 BINDING SITE, designated SEQ ID:32284, to the nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44380] Another function of VGAM1240 is therefore inhibition of LOC91012 (Accession XM_035503). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91012. LOC91380 (Accession XM_038134) is another VGAM1240 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32760, to the

nucleotide sequence of VGAM1240 RNA, herein designated VGAM RNA, also designated SEQ ID:3951.

[44381] Another function of VGAM1240 is therefore inhibition of LOC91380 (Accession XM_038134). Accordingly, utilities of VGAM1240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1241 (VGAM1241) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44382] VGAM1241 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1241 was detected is described hereinabove with reference to Figs. 1–8.

[44383] VGAM1241 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid Herpesvirus 3. VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44384] VGAM1241 gene encodes a VGAM1241 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1241 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1241 precursor RNA is designated SEQ ID:1227, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1227 is located at position 107745 relative to the genome of Gallid Herpesvirus 3.

[44385] VGAM1241 precursor RNA folds onto itself, forming VGAM1241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44386] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1241 folded precursor RNA into VGAM1241 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1241 RNA is designated SEQ ID:3952, and is provided hereinbelow with reference to the sequence listing part.

[44387] VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1241 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44388] VGAM1241 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1241 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1241 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44389] The complementary binding of VGAM1241 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1241 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1241 host target RNA into VGAM1241 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44390] It is appreciated that VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1241 host target genes. The mRNA of each one of this plurality of VGAM1241 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1241 RNA, herein designated VGAM RNA, and which when bound by VGAM1241 RNA causes inhibition of translation of respective one or more VGAM1241 host target proteins.

[44391] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1241 gene, herein designated VGAM GENE, on one or more VGAM1241 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[44392] It is yet further appreciated that a function of VGAM1241 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1241 include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1241 correlate with, and may be deduced from, the identity of the host target genes which VGAM1241 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44393] Nucleotide sequences of the VGAM1241 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1241 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1241 are further described hereinbelow with reference to Table 1.

[44394] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1241 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1241 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44395] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1241 gene, herein designated VGAM is inhibition of expression of VGAM1241 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1241 correlate with, and may be deduced from, the identity of the target genes which VGAM1241 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44396] PORIMIN (Accession NM_052932) is a VGAM1241 host target gene. PORIMIN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PORIMIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PORIMIN BINDING SITE, designated SEQ ID:27492, to the nucleotide sequence of VGAM1241 RNA, herein designated VGAM RNA, also designated SEQ ID:3952.

[44397] A function of VGAM1241 is therefore inhibition of PORIMIN (Accession NM_052932). Accordingly, utilities of

VGAM1241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PORIMIN. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1242 (VGAM1242) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44398] VGAM1242 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1242 was detected is described hereinabove with reference to Figs. 1–8.

[44399] VGAM1242 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid Herpesvirus 3. VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44400] VGAM1242 gene encodes a VGAM1242 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1242 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1242 precursor RNA is designated SEQ ID:1228, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1228 is located at position 101522 relative to the genome of Gallid Herpesvirus 3.

- [44401] VGAM1242 precursor RNA folds onto itself, forming VGAM1242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44402] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1242 folded precursor RNA into VGAM1242 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM1242 RNA is designated SEQ ID:3953, and

is provided hereinbelow with reference to the sequence listing part.

[44403] VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1242 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44404] VGAM1242 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1242 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1242 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44405] The complementary binding of VGAM1242 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1242 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1242 host target RNA into VGAM1242 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44406] It is appreciated that VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1242 host target genes. The mRNA of each one of this plurality of VGAM1242 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1242 RNA, herein designated VGAM RNA, and which when bound by VGAM1242 RNA causes inhibition of translation of respective one or more VGAM1242 host target proteins.

[44407] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1242 gene, herein designated VGAM GENE, on one or more VGAM1242 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44408] It is yet further appreciated that a function of VGAM1242 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM1242 correlate with, and may be deduced from, the identity of the host target genes which VGAM1242 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44409] Nucleotide sequences of the VGAM1242 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1242 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1242 are further described hereinbelow with reference to Table 1.

[44410] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1242 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1242 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44411] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1242 gene, herein designated VGAM is inhibition of expression of VGAM1242 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1242 correlate with, and may be deduced from, the identity of the target genes which VGAM1242 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44412] Carnitine O-octanoyltransferase (CROT, Accession NM_021151) is a VGAM1242 host target gene. CROT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CROT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CROT BINDING SITE, designated SEQ ID:22122, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44413] A function of VGAM1242 is therefore inhibition of Carnitine O-octanoyltransferase (CROT, Accession NM_021151), a gene which CROT plays a crucial role in the beta-oxidation of branched-chain fatty acids including pristanic acid. Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with CROT. The function of CROT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM70. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_001396) is another VGAM1242 host target gene. DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3, designated SEQ ID:7093, SEQ ID:28186 and SEQ ID:28163 respectively, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44414] Another function of VGAM1242 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_001396), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Unc-5 Homolog B (C. elegans) (UNC5C, Accession NM_003728) is another VGAM1242 host target gene. UNC5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC5C BINDING SITE, designated SEQ ID:9821, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44415] Another function of VGAM1242 is therefore inhibition of Unc-5 Homolog B (C. elegans) (UNC5C, Accession NM_003728), a gene which is a putative receptor for netrin, which is involved in axon guidance. Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5C. The function of UNC5C and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM298.KIAA0599 (Accession XM_085127) is another VGAM1242 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37853, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44416] Another function of VGAM1242 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. MGC11266 (Accession NM_024322) is another VGAM1242 host target gene. MGC11266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC11266 BINDING SITE, designated SEQ ID:23611, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44417] Another function of VGAM1242 is therefore inhibition of MGC11266 (Accession NM_024322). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11266. TUSP (Accession NM_020245) is another VGAM1242 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21539, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44418] Another function of VGAM1242 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. Zinc Finger Protein 262 (ZNF262, Accession NM_005095) is another VGAM1242 host target gene. ZNF262 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF262, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF262 BINDING SITE, designated SEQ ID:11556, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44419] Another function of VGAM1242 is therefore inhibition of Zinc Finger Protein 262 (ZNF262, Accession NM_005095). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF262. LOC147072 (Accession XM_017121) is another VGAM1242 host target gene. LOC147072 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147072 BINDING SITE, designated SEQ ID:30301, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44420] Another function of VGAM1242 is therefore inhibition of LOC147072 (Accession XM_017121). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147072. LOC147976 (Accession XM_085980) is another VGAM1242 host target gene. LOC147976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147976 BINDING SITE, designated SEQ ID:38429, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44421] Another function of VGAM1242 is therefore inhibition of LOC147976 (Accession XM_085980). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147976. LOC148645 (Accession XM_097492) is another VGAM1242 host target gene. LOC148645 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148645, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148645 BINDING SITE, designated SEQ ID:40891, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44422] Another function of VGAM1242 is therefore inhibition of LOC148645 (Accession XM_097492). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148645. LOC164397 (Accession XM_092780) is another VGAM1242 host target gene. LOC164397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164397 BINDING SITE, designated SEQ ID:40153, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44423] Another function of VGAM1242 is therefore inhibition of LOC164397 (Accession XM_092780). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC164397. LOC253985 (Accession XM_172875) is another VGAM1242 host target gene. LOC253985 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253985, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253985 BINDING SITE, designated SEQ ID:46151, to the nucleotide sequence of VGAM1242 RNA, herein designated VGAM RNA, also designated SEQ ID:3953.

[44424] Another function of VGAM1242 is therefore inhibition of LOC253985 (Accession XM_172875). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253985. LOC93444 (Accession XM_051455) is another VGAM1242 host target gene. LOC93444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93444 BINDING SITE, designated SEQ ID:35843, to the nucleotide sequence of VGAM1242 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3953.

[44425] Another function of VGAM1242 is therefore inhibition of LOC93444 (Accession XM_051455). Accordingly, utilities of VGAM1242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93444. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1243 (VGAM1243) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44426] VGAM1243 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1243 was detected is described hereinabove with reference to Figs. 1–8.

[44427] VGAM1243 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey Adenovirus 3. VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44428] VGAM1243 gene encodes a VGAM1243 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1243 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1243 precursor RNA is designated SEQ ID:1229, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1229 is located at position 18764 relative to the genome of Turkey Adenovirus 3.

- [44429] VGAM1243 precursor RNA folds onto itself, forming VGAM1243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44430] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1243 folded precursor RNA into VGAM1243 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1243 RNA is designated SEQ ID:3954, and is provided hereinbelow with reference to the sequence listing part.

[44431] VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1243 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44432] VGAM1243 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1243 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1243 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44433] The complementary binding of VGAM1243 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1243 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1243 host target RNA into VGAM1243 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44434] It is appreciated that VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1243 host target genes. The mRNA of

each one of this plurality of VGAM1243 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1243 RNA, herein designated VGAM RNA, and which when bound by VGAM1243 RNA causes inhibition of translation of respective one or more VGAM1243 host target proteins.

[44435] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1243 gene, herein designated VGAM GENE, on one or more VGAM1243 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[44436] It is yet further appreciated that a function of VGAM1243 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGAM1243 correlate with, and may be deduced from, the identity of the host target genes which VGAM1243 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44437] Nucleotide sequences of the VGAM1243 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1243 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1243 are further described hereinbelow with reference to Table 1.

[44438] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1243 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1243 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44439] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1243 gene, herein designated VGAM is inhibition of expression of VGAM1243 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1243 correlate with, and may be deduced from, the identity of the target genes which VGAM1243 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44440] Luteinizing Hormone/choriogonadotropin Receptor (LHCGR, Accession NM_000233) is a VGAM1243 host target gene. LHCGR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LHCGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHCGR BINDING SITE, designated SEQ ID:5744, to the nucleotide sequence of VGAM1243 RNA, herein designated VGAM RNA, also designated SEQ ID:3954.

[44441] A function of VGAM1243 is therefore inhibition of Luteinizing Hormone/choriogonadotropin Receptor

(LHCGR, Accession NM_000233). Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHCGR. Thymine–DNA Glycosylase (TDG, Accession NM_003211) is another VGAM1243 host target gene. TDG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TDG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TDG BINDING SITE, designated SEQ ID:9205, to the nucleotide sequence of VGAM1243 RNA, herein designated VGAM RNA, also designated SEQ ID:3954.

[44442] Another function of VGAM1243 is therefore inhibition of Thymine–DNA Glycosylase (TDG, Accession NM_003211), a gene which excises uracil and thymine from mispairs with guanine. Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TDG. The function of TDG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM196.KIAA1497 (Accession XM_041431) is another

VGAM1243 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33522, to the nucleotide sequence of VGAM1243 RNA, herein designated VGAM RNA, also designated SEQ ID:3954.

[44443] Another function of VGAM1243 is therefore inhibition of KIAA1497 (Accession XM_041431). Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1497. MGC12679 (Accession NM_032733) is another VGAM1243 host target gene. MGC12679 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12679, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12679 BINDING SITE, designated SEQ ID:26458, to the nucleotide sequence of VGAM1243 RNA, herein designated VGAM RNA, also designated SEQ ID:3954.

[44444] Another function of VGAM1243 is therefore inhibition of MGC12679 (Accession NM_032733). Accordingly, utilities of VGAM1243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12679. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1244 (VGAM1244) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44445] VGAM1244 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1244 was detected is described hereinabove with reference to Figs. 1-8.

[44446] VGAM1244 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey Adenovirus 3. VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44447] VGAM1244 gene encodes a VGAM1244 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1244 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1244 precursor RNA is designated SEQ ID:1230, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1230 is located at position 24452 relative to the genome of Turkey Adenovirus 3.

- [44448] VGAM1244 precursor RNA folds onto itself, forming VGAM1244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44449] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1244 folded precursor RNA into VGAM1244 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 74%) nucleotide sequence of VGAM1244 RNA is designated SEQ ID:3955, and is provided hereinbelow with reference to the sequence listing part.

[44450] VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1244 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[44451] VGAM1244 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1244 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1244 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44452] The complementary binding of VGAM1244 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1244 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1244 host target RNA into VGAM1244 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44453] It is appreciated that VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1244 host target genes. The mRNA of each one of this plurality of VGAM1244 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1244 RNA, herein designated VGAM RNA, and which when bound by VGAM1244 RNA causes inhibition of translation of respective one or more VGAM1244 host target proteins.

[44454] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1244 gene, herein designated VGAM GENE, on one or more VGAM1244 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44455] It is yet further appreciated that a function of VGAM1244 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1244 include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGAM1244 correlate with, and may be deduced from, the identity of the host target genes which VGAM1244 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44456] Nucleotide sequences of the VGAM1244 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1244 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1244 are further described hereinbelow with reference to Table 1.

[44457] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1244 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1244 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[44458] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1244 gene, herein designated VGAM is inhibition of expression of VGAM1244 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1244 correlate with, and may be deduced from, the identity of the target genes which VGAM1244 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44459] Coxsackie Virus and Adenovirus Receptor (CXADR, Accession NM_001338) is a VGAM1244 host target gene. CXADR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXADR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXADR BINDING SITE, designated SEQ ID:7018, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44460] A function of VGAM1244 is therefore inhibition of Coxsackie Virus and Adenovirus Receptor (CXADR, Accession NM_001338), a gene which is a member of the immunoglobulin superfamily. Accordingly, utilities of

VGAM1244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXADR. The function of CXADR has been established by previous studies. Bergelson et al. (1997) used immunoaffinity chromatography to purify a Coxsackie virus and adenovirus receptor protein, which they termed CAR. Based on the sequences of tryptic peptides, they cloned the corresponding cDNA from a HeLa cell library. The CAR cDNA encodes a predicted 365-amino acid polypeptide that contains a single transmembrane domain and is a member of the immunoglobulin superfamily. Bergelson et al. (1997) found that Chinese hamster cells bound to labeled Coxsackie viruses B3 and B4 and became susceptible to infection when transfected with CAR cDNA. Myocarditis and dilated cardiomyopathy are common causes of morbidity and mortality in children. Many studies have implicated the enteroviruses and particularly the Coxsackie virus B family as etiologic agents of the acquired forms of these diseases. However, Martin et al. (1994), Griffin et al. (1995), and Pauschinger et al. (1999) showed that the group C adenoviruses are as commonly detected as enteroviruses in the myocardium of children and adults with these diseases. The description of the common Coxsackie

virus B and adenovirus receptor offers a partial explanation for the observation that 2 such divergent virus families cause these diseases.

[44461] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44462] Bergelson, J. M.; Cunningham, J. A.; Droguett, G.; Kurt-Jones, E. A.; Krithivas, A.; Hong, J. S.; Horwitz, M. S.; Crowell, R. L.; Finberg, R. W. : Isolation of a common receptor for coxsackie B viruses and adenoviruses 2 and 5. Science 275: 1320–1323, 1997. ; and

[44463] Pauschinger, M.; Bowles, N. E.; Fuentes–Garcia, F. J.; Pham, V.; Kuhl, U.; Schwimmbeck, P. L.; Schultheiss, H.–P.; Towbin, J. A. : Detection of adenoviral genome in the myocardium of adu.

[44464] Further studies establishing the function and utilities of CXADR are found in John Hopkins OMIM database record ID 602621, and in cited publications numbered 8554–8560 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog 2 (mouse) (MEIS2, Accession NM_020149) is another VGAM1244 host target gene. MEIS2 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by MEIS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEIS2 BINDING SITE, designated SEQ ID:21345, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44465] Another function of VGAM1244 is therefore inhibition of Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog 2 (mouse) (MEIS2, Accession NM_020149), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEIS2. The function of MEIS2 has been established by previous studies. The Meis1 locus (OMIM Ref. No. 601739) was isolated as a common site of viral integration involved in myeloid leukemia in BXH-2 mice. Steelman et al. (1997) noted that MEIS1 encodes a homeo box protein belonging to the TALE ('three amino acid loop extension') family of homeodomain-containing proteins. The homeodomain of MEIS1 is the only conserved motif in the entire 390-amino acid protein. Steel-

man et al. (1997) reported that Southern blot analyses using the MEIS1 homeodomain as a probe revealed the existence of a family of Meis1-related genes (MRGs) in several divergent species. In addition, the 3-prime untranslated region (UTR) of MEIS1 is remarkably conserved in evolution. Steelman et al. (1997) cloned Meis1-related genes from the mouse and human genomes. One such gene, which the authors designated Mrg1, shares a similar genomic organization in the mouse with Meis1 but was found to be located on mouse chromosome 2, not mouse chromosome 11, where Meis1 maps. In humans, Steelman et al. (1997) mapped MRG1 to 15q22-q25 in a region associated with various cytogenetic abnormalities associated with acute myelocytic leukemia, chronic myeloid leukemia, and astrocytomas. The authors reported data suggesting that another related gene (MRG2) maps to human chromosome 17. During the course of their studies of the human MEIS1 homeo box gene, Smith et al. (1997) identified a gene closely related but not identical to MEIS1. Sequence analysis showed it to be the human counterpart of the mouse gene Meis2 (Nakamura et al., 1996). Human MEIS2 was found to be expressed in various human tissues. In hematopoietic tissues, the lymphoid organs expressed

high levels of MEIS2 as 2 transcripts of 4.0 kb and 3.5 kb. MEIS2 is also expressed in some regions of the brain, such as the putamen. Nakamura et al. (1996) mapped the mouse Meis2 gene to chromosome 2 in a region syntenic to human 15q. By fluorescence in situ hybridization with a genomic MEIS2 clone, Smith et al. (1997) mapped the human MEIS2 gene to a position that is 27% of the distance from the chromosome 15 centromere to the telomere, corresponding to 15q14. Capdevila et al. (1999) showed that restriction of expression of the chick homeobox gene Meis2 to proximal regions of the limb bud is essential for limb development, since ectopic Meis2 severely disrupted limb outgrowth. They also uncovered an antagonistic relationship between the secreted factor Gremlin (OMIM Ref. No. 603054) and the bone morphogenetic proteins (Bmps; OMIM Ref. No. 112264) that is required to maintain the Sonic hedgehog (OMIM Ref. No. 600725)/fibroblast growth factor (see OMIM Ref. No. 131220) loop that regulates distal outgrowth. These proximal and distal factors were found to have coordinated activities: Meis2 could repress distal genes, and the Bmp and Hoxd (OMIM Ref. No. 142987) genes restricted Meis2 expression to the proximal limb bud. Moreover, combinations of Bmps and apical

ectodermal ridge (AER) factors were sufficient to distalize proximal limb cells. These results unveiled a set of proximal–distal regulatory interactions that establish and maintain outgrowth of the vertebrate limb. Mercader et al. (1999) described the role of homeo box genes Meis1, Meis2, and Pbx1 (OMIM Ref. No. 176310) in the development of mouse, chicken, and Drosophila limbs. Mercader et al. (1999) found that Meis1 and Meis2 expression is restricted to the proximal domain, coincident with the previously reported domain in which Pbx1 is localized to the nucleus. Meis1 regulates Pbx1 activity by promoting nuclear import of the Pbx1 protein. Mercader et al. (1999) also demonstrated that ectopic expression of Meis1 in chicken disrupts distal limb development and induces distal-to-proximal transformations. Mercader et al. (1999) concluded that the restriction of Meis1 to proximal regions of the vertebrate limb is essential to specify cell fates and differentiation patterns along the proximodistal axis of the limb.

[44466] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44467] Capdevila, J.; Tsukui, T.; Esteban, C. R.; Zappavigna, V.;

Belmonte, J. C. I. : Control of vertebrate limb outgrowth by the proximal factor Meis2 and distal antagonism of BMPs by Gremlin. *Molec. Cell* 4: 839–849, 1999. ; and

[44468] Mercader, N.; Leonardo, E.; Azpiazu, N.; Serrano, A.; Morata, G.; Martinez–A, C.; Torres, M. : Conserved regulation of proximodistal limb axis development by Meis1/Hth. *Nature* 402: 425.

[44469] Further studies establishing the function and utilities of MEIS2 are found in John Hopkins OMIM database record ID 601740, and in cited publications numbered 9329, 10366–933 and 9405 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP564D172 (Accession NM_032042) is another VGAM1244 host target gene. DKFZP564D172 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564D172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D172 BINDING SITE, designated SEQ ID:25751, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44470] Another function of VGAM1244 is therefore inhibition of DKFZP564D172 (Accession NM_032042). Accordingly, utilities of VGAM1244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D172. HSMPP8 (Accession XM_167894) is another VGAM1244 host target gene. HSMPP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSMPP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSMPP8 BINDING SITE, designated SEQ ID:44901, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44471] Another function of VGAM1244 is therefore inhibition of HSMPP8 (Accession XM_167894). Accordingly, utilities of VGAM1244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSMPP8. Leucine-rich Repeat LGI Family, Member 4 (LGI4, Accession NM_139284) is another VGAM1244 host target gene. LGI4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LGI4, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGI4 BINDING SITE, designated SEQ ID:29287, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44472] Another function of VGAM1244 is therefore inhibition of Leucine-rich Repeat LGI Family, Member 4 (LGI4, Accession NM_139284). Accordingly, utilities of VGAM1244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LGI4. Mitogen-activated Protein Kinase 6 (MAPK6, Accession NM_002748) is another VGAM1244 host target gene. MAPK6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAPK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK6 BINDING SITE, designated SEQ ID:8625, to the nucleotide sequence of VGAM1244 RNA, herein designated VGAM RNA, also designated SEQ ID:3955.

[44473] Another function of VGAM1244 is therefore inhibition of Mitogen-activated Protein Kinase 6 (MAPK6, Accession NM_002748). Accordingly, utilities of VGAM1244 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK6. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1245 (VGAM1245) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44474] VGAM1245 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1245 was detected is described hereinabove with reference to Figs. 1–8.

[44475] VGAM1245 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey Adenovirus 3. VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44476] VGAM1245 gene encodes a VGAM1245 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1245 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1245 precursor RNA is desig-

nated SEQ ID:1231, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1231 is located at position 19532 relative to the genome of Turkey Adenovirus 3.

- [44477] VGAM1245 precursor RNA folds onto itself, forming VGAM1245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44478] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1245 folded precursor RNA into VGAM1245 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1245 RNA is designated SEQ ID:3956, and is provided hereinbelow with reference to the sequence

listing part.

[44479] VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1245 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44480] VGAM1245 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1245 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1245 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44481] The complementary binding of VGAM1245 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1245 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1245 host target RNA into VGAM1245 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44482] It is appreciated that VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1245 host target genes. The mRNA of each one of this plurality of VGAM1245 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1245 RNA, herein designated VGAM

RNA, and which when bound by VGAM1245 RNA causes inhibition of translation of respective one or more VGAM1245 host target proteins.

[44483] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1245 gene, herein designated VGAM GENE, on one or more VGAM1245 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44484] It is yet further appreciated that a function of VGAM1245 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1245 include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGAM1245 correlate with, and may be deduced from, the identity of the host target genes which VGAM1245 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44485] Nucleotide sequences of the VGAM1245 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1245 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1245 are further described hereinbelow with reference to Table 1.

[44486] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1245 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1245 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44487] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1245 gene, herein designated VGAM is

inhibition of expression of VGAM1245 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1245 correlate with, and may be deduced from, the identity of the target genes which VGAM1245 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44488] Arylsulfatase D (ARSD, Accession NM_009589) is a VGAM1245 host target gene. ARSD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARSD BINDING SITE, designated SEQ ID:14316, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44489] A function of VGAM1245 is therefore inhibition of Arylsulfatase D (ARSD, Accession NM_009589), a gene which hydrolyzes sulfate groups from sugar residues in complex glycoconjugates. Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARSD. The function of ARSD and its association with various diseases and clinical

conditions, has been established by previous studies, as described hereinabove with reference to VGAM232.V-erb-a Erythroblastic Leukemia Viral Oncogene Homolog 4 (avian) (ERBB4, Accession NM_005235) is another VGAM1245 host target gene. ERBB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERBB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERBB4 BINDING SITE, designated SEQ ID:11746, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44490] Another function of VGAM1245 is therefore inhibition of V-erb-a Erythroblastic Leukemia Viral Oncogene Homolog 4 (avian) (ERBB4, Accession NM_005235), a gene which may function in growth/differentiation of normal and transformed cells. Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERBB4. The function of ERBB4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM381.Galanin Receptor 1 (GALR1, Accession NM_001480) is another VGAM1245 host target gene. GALR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALR1 BINDING SITE, designated SEQ ID:7215, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44491] Another function of VGAM1245 is therefore inhibition of Galanin Receptor 1 (GALR1, Accession NM_001480), a gene which plays a role in regulating ion transport. Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALR1. The function of GALR1 has been established by previous studies. Galanin (OMIM Ref. No. 137035) is an important neuromodulator present in the brain, gastrointestinal system, and hypothalamopituitary axis. It is a 30-amino acid non-C-terminally amidated peptide that potently stimulates growth hormone secretion, inhibits cardiac vagal slowing of heart rate, abolishes

sinus arrhythmia, and inhibits postprandial gastrointestinal motility. The actions of galanin are mediated through interaction with specific membrane receptors that are members of the 7-transmembrane family of G protein-coupled receptors. Walli et al. (1994) identified and biochemically characterized a specific receptor for galanin in various areas of human brain. Habert-Ortoli et al. (1994) also cloned a functional human galanin receptor. Hecht et al. (1999) showed that pathogenic *E. coli*, but not normal commensal organisms, increase GALR1, which they called GAL1R, mRNA synthesis and (125)I-galanin binding sites. In mice infected with enterohemorrhagic *E. coli* by gavage, infection caused a progressive increase in both nuclear factor kappa-B (see OMIM Ref. No. 164011) activation and GALR1 expression, with maximal levels of both observed 3 days after gavage. With Ussing chamber studies, they showed that colons infected with enterohemorrhagic *E. coli*, but not those exposed to normal colonic flora, markedly increased short-circuit current in response to galanin. These data indicated that pathogen-induced increases in GALR1 expression by epithelial cells lining the colon represent a novel unifying pathway responsible for at least a portion of the excessive fluid secretion observed

during infectious diarrhea.

[44492] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44493] Hecht, G.; Marrero, J. A.; Danilkovich, A.; Matkowskyj, K. A.; Savkovic, S. D.; Koutsouris, A.; Benya, R. V. : Pathogenic *Escherichia coli* increase Cl⁻ secretion from intestinal epithelia by upregulating galanin-1 receptor expression. *J. Clin. Invest.* 104: 253-262, 1999. ; and

[44494] Jacoby, A. S.; Webb, G. C.; Liu, M. L.; Kofler, B.; Hort, Y. J.; Fathi, Z.; Bottema, C. D. K.; Shine, J.; Iismaa, T. P. : Structural organization of the mouse and human GALR1 galanin r.

[44495] Further studies establishing the function and utilities of GALR1 are found in John Hopkins OMIM database record ID 600377, and in cited publications numbered 1627-1629, 1025 and 10376-10380 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10204 (Accession NM_018024) is another VGAM1245 host target gene. FLJ10204 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10204, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10204 BINDING SITE, designated SEQ ID:19765, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44496] Another function of VGAM1245 is therefore inhibition of FLJ10204 (Accession NM_018024). Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10204. FLJ21272 (Accession NM_025032) is another VGAM1245 host target gene. FLJ21272 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21272, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21272 BINDING SITE, designated SEQ ID:24629, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44497] Another function of VGAM1245 is therefore inhibition of FLJ21272 (Accession NM_025032). Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ21272. KIAA0461 (Accession XM_047883) is another VGAM1245 host target gene. KIAA0461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0461 BINDING SITE, designated SEQ ID:35072, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44498] Another function of VGAM1245 is therefore inhibition of KIAA0461 (Accession XM_047883). Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0461. LOC150139 (Accession XM_086794) is another VGAM1245 host target gene. LOC150139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150139 BINDING SITE, designated SEQ ID:38858, to the nucleotide sequence of VGAM1245 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:3956.

[44499] Another function of VGAM1245 is therefore inhibition of LOC150139 (Accession XM_086794). Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150139. LOC150481 (Accession XM_086929) is another VGAM1245 host target gene. LOC150481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150481 BINDING SITE, designated SEQ ID:38978, to the nucleotide sequence of VGAM1245 RNA, herein designated VGAM RNA, also designated SEQ ID:3956.

[44500] Another function of VGAM1245 is therefore inhibition of LOC150481 (Accession XM_086929). Accordingly, utilities of VGAM1245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150481. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1246 (VGAM1246) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44501] VGAM1246 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1246 was detected is described hereinabove with reference to Figs. 1–8.

[44502] VGAM1246 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Turkey Adenovirus 3. VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44503] VGAM1246 gene encodes a VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1246 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1246 precursor RNA is designated SEQ ID:1232, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1232 is located at position 24059 relative to the genome of Turkey Adenovirus 3.

[44504] VGAM1246 precursor RNA folds onto itself, forming

VGAM1246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44505] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1246 folded precursor RNA into VGAM1246 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1246 RNA is designated SEQ ID:3957, and is provided hereinbelow with reference to the sequence listing part.

[44506] VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1246 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44507] VGAM1246 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1246 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1246 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44508] The complementary binding of VGAM1246 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1246 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1246 host target RNA into VGAM1246 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44509] It is appreciated that VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1246 host target genes. The mRNA of each one of this plurality of VGAM1246 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1246 RNA, herein designated VGAM RNA, and which when bound by VGAM1246 RNA causes inhibition of translation of respective one or more VGAM1246 host target proteins.

[44510] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1246 gene, herein designated VGAM GENE, on one or more VGAM1246 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44511] It is yet further appreciated that a function of VGAM1246 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGAM1246 correlate with, and may be deduced from, the identity of the host target genes which VGAM1246 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[44512] Nucleotide sequences of the VGAM1246 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1246 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1246 are further described hereinbelow with reference to Table 1.

[44513] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1246 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1246 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44514] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1246 gene, herein designated VGAM is inhibition of expression of VGAM1246 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1246 correlate with, and may be deduced from, the identity of the target genes which VGAM1246 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[44515] ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 12 (ABCC12, Accession NM_033226) is a VGAM1246 host target gene. ABCC12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCC12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC12 BINDING SITE, designated SEQ ID:27073, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44516] A function of VGAM1246 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 12 (ABCC12, Accession NM_033226), a gene which acts as a multispecific organic anion pump which can transport nucleotide analogs (by similarity). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC12. The function of ABCC12 has been established by previous studies. Tammur et al. (2001) identified ABCC12 and ABCC11 (OMIM Ref. No. 607040) by database analysis using ABC transporter sequences as queries. The deduced

1,359–amino acid ABCC12 protein contains 2 ATP–binding domains and 2 transmembrane regions. It shares 42% amino acid sequence identity with ABCC5 (OMIM Ref. No. 605251). PCR of a 16–tissue panel revealed expression only in testis, ovary, and prostate. Bera et al. (2002) detected expression in testis, pancreas, ovary, skeletal muscle, and various brain regions. Northern blot and dot blot analyses using variant–specific probes revealed a 4.5–kb transcript expressed in testis, normal breast, and breast cancer tissues, and a 1.3–kb transcript in brain, skeletal muscle, and ovary. In situ hybridization of normal and cancerous breast tissue revealed stronger staining in tumor cells. Tammur et al. (2001) mapped the ABCC12 gene to chromosome 16q12.1 by radiation hybrid analysis and by the presence of ABCC12 within a BAC clone. They stated that chromosomal localization, potential function, and expression profiles of the ABCC11 and ABCC12 genes make them promising candidates for paroxysmal kinesigenic choreoathetosis (PKC; 128200) and infantile convulsions with paroxysmal choreoathetosis (ICCA; 602066).

[44517] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [44518] Tammur, J.; Prades, C.; Arnould, I.; Rzhetsky, A.; Hutchinson, A.; Adachi, M.; Schuetz, J. D.; Swoboda, K. J.; Ptacek, L. J.; Rosier, M.; Dean, M.; Allikmets, R. : Two new genes from the human ATP-binding cassette transporter superfamily, ABCC11 and ABCC12, tandemly duplicated on chromosome 16q12. *Gene* 273: 89–96, 2001. ; and
- [44519] Bera, T. K.; Iavarone, C.; Kumar, V.; Lee, S.; Lee, B.; Pastan, I. : MRP9, an unusual truncated member of the ABC transporter superfamily, is highly expressed in breast cancer. *Proc. Natl. Acad. Sci. USA* 98: 1051–1056, 2001.
- [44520] Further studies establishing the function and utilities of ABCC12 are found in John Hopkins OMIM database record ID 607041, and in cited publications numbered 5171–5166 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Beclin 1 (coiled-coil, myosin-like BCL2 interacting protein) (BECN1, Accession NM_003766) is another VGAM1246 host target gene. BECN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BECN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BECN1 BINDING SITE, designated SEQ

ID:9843, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44521] Another function of VGAM1246 is therefore inhibition of Beclin 1 (coiled-coil, myosin-like BCL2 interacting protein) (BECN1, Accession NM_003766), a gene which protects cell from viral-induced apoptosis. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BECN1. The function of BECN1 has been established by previous studies. The process of autophagy, or bulk degradation of cellular proteins through an autophagosomic-lysosomal pathway, is important in normal growth control and may be defective in tumor cells. However, little is known about the genetic mediators of autophagy in mammalian cells or their role in tumor development. Beclin-1 was found to have structural similarity to the yeast autophagy gene, *apg6/vps30*, and is monoallelically deleted in 40 to 75% of sporadic human breast cancers and ovarian cancers. Liang et al. (1999) used gene transfer techniques to demonstrate that beclin-1 promotes autophagy in autophagy-defective yeast with a targeted disruption of *apg6/vps30*, and in human MCF7 breast carcinoma cells. The au-

tophagy-promoting activity of beclin-1 in MCF7 cells was associated with inhibition of MCF7 cellular proliferation, in vitro clonogenicity, and tumorigenesis in nude mice. Furthermore, endogenous beclin-1 protein expression is frequently low in human breast epithelial carcinoma cell lines and tissue, but is ubiquitous at high levels in normal breast epithelia. Thus, Liang et al. (1999) concluded that beclin-1 is a mammalian autophagy gene that can inhibit tumorigenesis and is expressed at decreased levels in human breast carcinoma. Liang et al. (1999) suggested that decreased expression of autophagy proteins may contribute to the development or progression of breast and other human malignancies. Short leucine-rich nuclear export signals (NESs), which were first identified in the human immunodeficiency virus-1 (HIV-1) Rev protein, are found in viral and cellular proteins required for RNA export. The NES forms a complex with CRM1 (OMIM Ref. No. 602559), the nuclear export receptor, and RanGTP (see OMIM Ref. No. 602362). Complex formation can be blocked by the fungicide leptomycin B. By structural analysis, Liang et al. (2001) identified an NES at positions 180 to 189 in BECN1. Fluorescence microscopy demonstrated nuclear and cytoplasmic expression of wildtype BECN1,

while leptomycin B-treated BECN1 or BECN1 carrying leucine mutations in its NES were expressed only in the nucleus. Mutant BECN1 was unable to promote basal or nutrient deprivation-induced autophagy and was unable to suppress growth of breast cancer cells in vitro or in vivo. Liang et al. (2001) suggested that the nuclear export pathway may be important in the functional regulation of autophagic growth control.

[44522] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44523] Liang, X. H.; Jackson, S.; Seaman, M.; Brown, K.; Kempkes, B.; Hibshoosh, H.; Levine, B. : Induction of autophagy and inhibition of tumorigenesis by beclin 1. Nature 402: 672–676, 1999. ; and

[44524] Liang, X. H.; Yu, J.; Brown, K.; Levine, B. : Beclin 1 contains a leucine-rich nuclear export signal that is required for its autophagy and tumor suppressor function. Cancer Res. 61: 34.

[44525] Further studies establishing the function and utilities of BECN1 are found in John Hopkins OMIM database record ID 604378, and in cited publications numbered 7073–7076 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Cysteine Dioxygenase, Type I (CDO1, Accession NM_001801) is another VGAM1246 host target gene. CDO1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDO1 BINDING SITE, designated SEQ ID:7556, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44526] Another function of VGAM1246 is therefore inhibition of Cysteine Dioxygenase, Type I (CDO1, Accession NM_001801), a gene which is involved in degradation of cysteine to pyruvate. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDO1. The function of CDO1 has been established by previous studies. The first step in the oxidation of cysteine to inorganic sulphate is its conversion to cysteine sulphinate by cysteine dioxygenase (CDO; EC 1.13.11.20). In rat, at least 2 enzymes catalyze this reaction, one cytosolic (CDO-I) and the other membrane-bound. Rat liver CDO contains 1

atom of iron per molecule of protein, and the enzyme is activated by anaerobic incubation with either L-cysteine or its analogs. Hosokawa et al. (1990) isolated rat liver cDNAs encoding the cytosolic CDO. The protein's predicted molecular weight of 23 kD was in good agreement with its apparent molecular mass by SDS-PAGE. By screening a human liver library with a rat CDO-I cDNA, McCann et al. (1994) identified human CDO-I cDNAs. The predicted 200-amino acid human and rat proteins are 94% identical. Northern blot analysis revealed that CDO-I is expressed as an approximately 1.5-kb mRNA in liver. Ramsden et al. (1997) reported that the human CDO-I gene contains 5 exons and spans more than 12 kb. By analysis of somatic cell hybrids and by fluorescence in situ hybridization, Jeremiah et al. (1996) mapped the CDO1 gene to human chromosome 5q22-q23. Using an interspecific backcross, these authors mapped the mouse homolog to the central region of mouse chromosome 18, in a region sharing homology of synteny with human chromosome 5.

[44527] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44528] Hosokawa, Y.; Matsumoto, A.; Oka, J.; Itakura, H.; Yam-

aguchi, K. : Isolation and characterization of a cDNA for rat liver cysteine dioxygenase. Biochem. Biophys. Res. Commun. 168: 473–478, 1990. ; and

[44529] Jeremiah, S.; McCann, K. P.; Williams, A. C.; Ramsden, D. B.; Pilz, A. J.; Fox, M. F.; Povey, S. : Chromosomal localisation of genes coding for human and mouse liver cytosolic cysteine.

[44530] Further studies establishing the function and utilities of CDO1 are found in John Hopkins OMIM database record ID 603943, and in cited publications numbered 5192–519 and 5169 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Drebrin 1 (DBN1, Accession NM_004395) is another VGAM1246 host target gene. DBN1 BINDING SITE1 and DBN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DBN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DBN1 BINDING SITE1 and DBN1 BINDING SITE2, designated SEQ ID:10640 and SEQ ID:28125 respectively, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44531] Another function of VGAM1246 is therefore inhibition of Drebrin 1 (DBN1, Accession NM_004395). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DBN1. FUS1 (Accession NM_007275) is another VGAM1246 host target gene. FUS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUS1 BINDING SITE, designated SEQ ID:14138, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44532] Another function of VGAM1246 is therefore inhibition of FUS1 (Accession NM_007275), a gene which may function as a tumor suppressor. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUS1. The function of FUS1 has been established by previous studies. Lerman and Minna (2000) identified a FUS1 mutation in 2 nonsmall cell lung cancer (NSCLC) cell lines that resulted in a 28-bp truncation at the 3-prime end of exon

2 and a predicted protein of only 82 amino acids. Using SSCP and CpG island promoter methylation analyses, Kondo et al. (2001) failed to detect mutations, polymorphisms, or methylation of FUS1 in lung cancer specimens. Western blot analysis indicated low or no expression of FUS1 in lung cancer cell lines. Overexpression of transfected wildtype but not mutant FUS1 in NSCLCs led to the detection of an approximately 20-kD protein and a dramatic reduction in colony-forming cells. Ecdysone-induced expression of FUS1 had the same effects. Flow cytometric analysis indicated that the arrest occurred in G1 phase.

[44533] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44534] Kondo, M.; Ji, L.; Kamibayashi, C.; Tomizawa, Y.; Randle, D.; Sekido, Y.; Yokota, J.; Kashuba, V.; Zabarovsky, E.; Kuzmin, I.; Lerman, M.; Roth, J.; Minna, J. D. : Overexpression of candidate tumor suppressor gene FUS1 isolated from the 3p21.3 homozygous deletion region leads to G1 arrest and growth inhibition of lung cancer cells. *Oncogene* 20: 6258–6262, 2001. ; and

[44535] Lerman, M. I.; Minna, J. D. : The 630-kb lung cancer ho-

mozygous deletion region on human chromosome 3p21.3: identification and evaluation of the resident candidate tumor suppressor gen.

[44536] Further studies establishing the function and utilities of FUS1 are found in John Hopkins OMIM database record ID 607052, and in cited publications numbered 5388 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 4, Regulatory Subunit 1 (PPP4R1, Accession NM_005134) is another VGAM1246 host target gene. PPP4R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP4R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP4R1 BINDING SITE, designated SEQ ID:11610, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44537] Another function of VGAM1246 is therefore inhibition of Protein Phosphatase 4, Regulatory Subunit 1 (PPP4R1, Accession NM_005134). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP4R1. Retinoic

Acid Induced 3 (RAI3, Accession NM_003979) is another VGAM1246 host target gene. RAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI3 BINDING SITE, designated SEQ ID:10113, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44538] Another function of VGAM1246 is therefore inhibition of Retinoic Acid Induced 3 (RAI3, Accession NM_003979). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI3. Transcription Factor 19 (SC1) (TCF19, Accession XM_175167) is another VGAM1246 host target gene. TCF19 BINDING SITE1 and TCF19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF19 BINDING SITE1 and TCF19 BINDING SITE2, desig-

nated SEQ ID:46660 and SEQ ID:46709 respectively, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44539] Another function of VGAM1246 is therefore inhibition of Transcription Factor 19 (SC1) (TCF19, Accession XM_175167), a gene which plays an important role in the transcription of genes required for the later stages of cell cycle progression. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF19. The function of TCF19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM299. UPF3A (Accession NM_023011) is another VGAM1246 host target gene. UPF3A BINDING SITE1 and UPF3A BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UPF3A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UPF3A BINDING SITE1 and UPF3A BINDING SITE2, designated SEQ ID:23275 and SEQ ID:33765 respectively, to the nucleotide sequence of VGAM1246 RNA,

herein designated VGAM RNA, also designated SEQ ID:3957.

[44540] Another function of VGAM1246 is therefore inhibition of UPF3A (Accession NM_023011), a gene which facilitates the export of spliced mRNAs by recruiting mRNA export proteins. Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UPF3A. The function of UPF3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM360.FLJ12747 (Accession NM_032173) is another VGAM1246 host target gene. FLJ12747 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12747 BINDING SITE, designated SEQ ID:25881, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44541] Another function of VGAM1246 is therefore inhibition of FLJ12747 (Accession NM_032173). Accordingly, utilities of

VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12747. FLJ20313 (Accession NM_017762) is another VGAM1246 host target gene. FLJ20313 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20313 BINDING SITE, designated SEQ ID:19377, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44542] Another function of VGAM1246 is therefore inhibition of FLJ20313 (Accession NM_017762). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20313. KIAA0237 (Accession NM_014747) is another VGAM1246 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0237 BINDING SITE, designated SEQ ID:16449, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44543] Another function of VGAM1246 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. Ring Finger Protein 10 (RNF10, Accession NM_014868) is another VGAM1246 host target gene. RNF10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RNF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF10 BINDING SITE, designated SEQ ID:16964, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44544] Another function of VGAM1246 is therefore inhibition of Ring Finger Protein 10 (RNF10, Accession NM_014868). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF10. Solute Carrier Family 31

(copper transporters), Member 2 (SLC31A2, Accession XM_011776) is another VGAM1246 host target gene. SLC31A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC31A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC31A2 BINDING SITE, designated SEQ ID:30194, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44545] Another function of VGAM1246 is therefore inhibition of Solute Carrier Family 31 (copper transporters), Member 2 (SLC31A2, Accession XM_011776). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC31A2. LOC115297 (Accession XM_053313) is another VGAM1246 host target gene. LOC115297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC115297 BINDING SITE, designated SEQ ID:36074, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44546] Another function of VGAM1246 is therefore inhibition of LOC115297 (Accession XM_053313). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115297. LOC115817 (Accession NM_138452) is another VGAM1246 host target gene. LOC115817 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115817 BINDING SITE, designated SEQ ID:28814, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44547] Another function of VGAM1246 is therefore inhibition of LOC115817 (Accession NM_138452). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115817. LOC126755 (Accession XM_059074) is another VGAM1246 host target gene. LOC126755 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC126755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126755 BINDING SITE, designated SEQ ID:36858, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44548] Another function of VGAM1246 is therefore inhibition of LOC126755 (Accession XM_059074). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126755. LOC200014 (Accession XM_114087) is another VGAM1246 host target gene. LOC200014 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42692, to the nucleotide sequence of VGAM1246 RNA, herein designated VGAM RNA, also designated SEQ ID:3957.

[44549] Another function of VGAM1246 is therefore inhibition of

LOC200014 (Accession XM_114087). Accordingly, utilities of VGAM1246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1247 (VGAM1247) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44550] VGAM1247 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1247 was detected is described hereinabove with reference to Figs. 1-8.

[44551] VGAM1247 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44552] VGAM1247 gene encodes a VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1247 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1247 precursor RNA is designated SEQ ID:1233, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1233 is located at position 132081 relative to the genome of Monkeypox Virus.

- [44553] VGAM1247 precursor RNA folds onto itself, forming VGAM1247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44554] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1247 folded precursor RNA into VGAM1247 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM1247 RNA is designated SEQ ID:3958, and is provided hereinbelow with reference to the sequence listing part.

[44555] VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1247 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44556] VGAM1247 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1247 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1247 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[44557] The complementary binding of VGAM1247 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1247 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1247 host target RNA into VGAM1247 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44558] It is appreciated that VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1247 host target genes. The mRNA of each one of this plurality of VGAM1247 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1247 RNA, herein designated VGAM RNA, and which when bound by VGAM1247 RNA causes inhibition of translation of respective one or more VGAM1247 host target proteins.

[44559] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1247 gene, herein designated VGAM GENE, on one or more VGAM1247 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44560] It is yet further appreciated that a function of VGAM1247

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1247 correlate with, and may be deduced from, the identity of the host target genes which VGAM1247 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44561] Nucleotide sequences of the VGAM1247 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1247 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1247 are further described hereinbelow with reference to Table 1.

[44562] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1247 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1247 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44563] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1247 gene, herein designated VGAM is inhibition of expression of VGAM1247 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1247 correlate with, and may be deduced from, the identity of the target genes which VGAM1247 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44564] Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM_054027) is a VGAM1247 host target gene. ANKH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKH BINDING SITE, designated SEQ ID:27638, to the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, also designated SEQ ID:3958.

[44565] A function of VGAM1247 is therefore inhibition of Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM_054027), a gene which regulates intra- and extracellular levels of inorganic pyrophosphate (ppi), probably functioning as ppi transporter. Accordingly, utilities of

VGAM1247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKH. The function of ANKH has been established by previous studies. Craniometaphyseal dysplasia (CMD; 123000) is a bone dysplasia characterized by overgrowth and sclerosis of the craniofacial bones and abnormal modeling of the metaphyses of the tubular bones. Hyperostosis and sclerosis of the skull may lead to cranial nerve compressions resulting in hearing loss and facial palsy. An autosomal dominant form of the disorder was mapped to 5p15.2–p14.1 (Nurnberg et al., 1997) within a region harboring the human homolog (ANKH) of the mouse progressive ankylosis (ank) gene. The ANK protein spans the outer cell membrane and shuttles inorganic pyrophosphate, a major inhibitor of physiologic and pathologic calcification, bone mineralization, and bone resorption. Nurnberg et al. (2001) identified 6 different mutations in the ANKH gene in 8 of 9 families with CMD. The mutations predicted single amino acid substitutions, deletions, or insertions. Using a helix prediction program, they proposed for the ANK molecule 12 membrane-spanning helices with an alternate inside/out orientation and a central channel permitting the passage of inorganic pyrophos-

phate. The mutations occurred at highly conserved amino acid residues presumed to be located in the cytosolic portion of the protein. The results linked the inorganic pyrophosphate channel ANK with bone formation and remodeling. Animal model experiments lend further support to the function of ANKH. Mice carrying the progressive ankylosis mutation have been studied as a model of arthritis. The autosomal recessive Ank mutation causes an abnormal flat-footed gait in young mice due to decreased mobility of ankle and toe joints. Loss of joint mobility becomes more severe with age and spreads to most joints throughout the limbs and vertebral column leading to complete rigidity and death around 6 months of age. Hydroxyapatite crystals develop in articular surfaces and synovial fluid of Ank mice, accompanied by joint space narrowing, cartilage erosion, and formation of bony outgrowths or osteophytes that cause fusion (ankylosis) and joint immobility. Ho et al. (2000) identified a G-to-T substitution in the mouse Ank gene, leading to a nonsense mutation in exon 11, the penultimate exon of mouse Ank. This mutation truncates the C-terminal region of the protein and greatly reduces its activity in vitro. The mouse Ank gene is expressed in developing articular surfaces

and may help maintain the unmineralized state by providing a local source of inorganic pyrophosphate to inhibit hydroxyapatite formation. In the absence of normal Ank activity, mineralization extends unhindered throughout articular cartilage, hydroxyapatite deposits form in synovial fluid, and new bone is deposited in and around joints, showing that the gene is essential for normal joint maintenance.

[44566] It is appreciated that the abovementioned animal model for ANKH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[44567] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44568] Ho, A. M.; Johnson, M. D.; Kingsley, D. M. : Role of the mouse ank gene in control of tissue calcification and arthritis. Science 289: 265–270, 2000. ; and

[44569] Nurnberg, P.; Tinschert, S.; Mrug, M.; Hampe, J.; Muller, C. R.; Fuhrmann, E.; Braun, H.–S.; Reis, A. : The gene for autosomal dominant craniometaphyseal dysplasia maps to chromosome 5q.

[44570] Further studies establishing the function and utilities of

ANKH are found in John Hopkins OMIM database record ID 605145, and in cited publications numbered 2877, 3552–355 and 7300 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Beta 4 (PCDHB4, Accession NM_018938) is another VGAM1247 host target gene. PCDHB4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDHB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB4 BINDING SITE, designated SEQ ID:21005, to the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, also designated SEQ ID:3958.

[44571] Another function of VGAM1247 is therefore inhibition of Protocadherin Beta 4 (PCDHB4, Accession NM_018938). Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB4. Zinc Finger Protein 266 (ZNF266, Accession XM_113992) is another VGAM1247 host target gene. ZNF266 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by ZNF266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF266 BINDING SITE, designated SEQ ID:42598, to the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, also designated SEQ ID:3958.

[44572] Another function of VGAM1247 is therefore inhibition of Zinc Finger Protein 266 (ZNF266, Accession XM_113992). Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF266. KIAA0293 (Accession XM_027045) is another VGAM1247 host target gene. KIAA0293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0293 BINDING SITE, designated SEQ ID:30391, to the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, also designated SEQ ID:3958.

[44573] Another function of VGAM1247 is therefore inhibition of

KIAA0293 (Accession XM_027045). Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0293. LOC163026 (Accession XM_091942) is another VGAM1247 host target gene. LOC163026 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163026 BINDING SITE, designated SEQ ID:40071, to the nucleotide sequence of VGAM1247 RNA, herein designated VGAM RNA, also designated SEQ ID:3958.

[44574] Another function of VGAM1247 is therefore inhibition of LOC163026 (Accession XM_091942). Accordingly, utilities of VGAM1247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163026. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1248 (VGAM1248) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[44575] VGAM1248 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1248 was detected is described hereinabove with reference to Figs. 1–8.

[44576] VGAM1248 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44577] VGAM1248 gene encodes a VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1248 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1248 precursor RNA is designated SEQ ID:1234, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1234 is located at position 131818 relative to the genome of Monkeypox Virus.

[44578] VGAM1248 precursor RNA folds onto itself, forming VGAM1248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44579] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1248 folded precursor RNA into VGAM1248 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM1248 RNA is designated SEQ ID:3959, and is provided hereinbelow with reference to the sequence listing part.

[44580] VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1248 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44581] VGAM1248 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1248 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1248 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[44582] The complementary binding of VGAM1248 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1248 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1248 host target RNA into VGAM1248 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44583] It is appreciated that VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1248 host target genes. The mRNA of each one of this plurality of VGAM1248 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1248 RNA, herein designated VGAM RNA, and which when bound by VGAM1248 RNA causes inhibition of translation of respective one or more VGAM1248 host target proteins.

[44584] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1248 gene, herein designated VGAM GENE, on one

or more VGAM1248 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44585] It is yet further appreciated that a function of VGAM1248 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1248 correlate with, and may be deduced from, the identity of the host target genes which VGAM1248 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44586] Nucleotide sequences of the VGAM1248 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1248 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1248 are further described hereinbelow with reference to Table 1.

[44587] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1248 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1248 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44588] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1248 gene, herein designated VGAM is inhibition of expression of VGAM1248 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1248 correlate with, and may be deduced from, the identity of the target genes which VGAM1248 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44589] BDG-29 (Accession XM_051343) is a VGAM1248 host tar-

get gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35816, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44590] A function of VGAM1248 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BDG-29. Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940) is another VGAM1248 host target gene. C21orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf6 BINDING SITE, designated SEQ ID:18855, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ

ID:3959.

[44591] Another function of VGAM1248 is therefore inhibition of Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf6. DKFZp434D177 (Accession NM_032264) is another VGAM1248 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:26007, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44592] Another function of VGAM1248 is therefore inhibition of DKFZp434D177 (Accession NM_032264). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434D177. HSA249128 (Accession NM_017583) is another VGAM1248 host target gene. HSA249128

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19027, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44593] Another function of VGAM1248 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA249128. KIAA1634 (Accession XM_032749) is another VGAM1248 host target gene. KIAA1634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1634 BINDING SITE, designated SEQ ID:31751, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44594] Another function of VGAM1248 is therefore inhibition of KIAA1634 (Accession XM_032749). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1634. KIAA1941 (Accession XM_059318) is another VGAM1248 host target gene. KIAA1941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1941 BINDING SITE, designated SEQ ID:36951, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44595] Another function of VGAM1248 is therefore inhibition of KIAA1941 (Accession XM_059318). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1941. PRO2533 (Accession NM_018629) is another VGAM1248 host target gene. PRO2533 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2533 BINDING SITE, designated SEQ ID:20702, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44596] Another function of VGAM1248 is therefore inhibition of PRO2533 (Accession NM_018629). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2533. LOC151201 (Accession XM_098021) is another VGAM1248 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41323, to the nucleotide sequence of VGAM1248 RNA, herein designated VGAM RNA, also designated SEQ ID:3959.

[44597] Another function of VGAM1248 is therefore inhibition of LOC151201 (Accession XM_098021). Accordingly, utilities of VGAM1248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC151201. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1249 (VGAM1249) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44598] VGAM1249 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1249 was detected is described hereinabove with reference to Figs. 1–8.

[44599] VGAM1249 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44600] VGAM1249 gene encodes a VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1249 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1249 precursor RNA is designated SEQ ID:1235, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1235 is located at position 130478 relative to the genome of Monkeypox Virus.

- [44601] VGAM1249 precursor RNA folds onto itself, forming VGAM1249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44602] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1249 folded precursor RNA into VGAM1249 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1249 RNA is designated SEQ ID:3960, and is provided hereinbelow with reference to the sequence listing part.

[44603] VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1249 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44604] VGAM1249 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1249 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1249 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[44605] The complementary binding of VGAM1249 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1249 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1249 host target RNA into VGAM1249 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44606] It is appreciated that VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1249 host target genes. The mRNA of each one of this plurality of VGAM1249 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1249 RNA, herein designated VGAM RNA, and which when bound by VGAM1249 RNA causes

inhibition of translation of respective one or more VGAM1249 host target proteins.

[44607] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1249 gene, herein designated VGAM GENE, on one or more VGAM1249 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44608] It is yet further appreciated that a function of VGAM1249 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1249 include diagnosis, prevention and

treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1249 correlate with, and may be deduced from, the identity of the host target genes which VGAM1249 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44609] Nucleotide sequences of the VGAM1249 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1249 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1249 are further described hereinbelow with reference to Table 1.

[44610] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1249 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1249 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44611] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1249 gene, herein designated VGAM is inhibition of expression of VGAM1249 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1249 correlate with, and may be deduced from, the identity of the target genes which VGAM1249 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44612] Bullous Pemphigoid Antigen 1, 230/240kDa (BPAG1, Accession NM_015548) is a VGAM1249 host target gene. BPAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BPAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BPAG1 BINDING SITE, designated SEQ ID:17811, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44613] A function of VGAM1249 is therefore inhibition of Bullous Pemphigoid Antigen 1, 230/240kDa (BPAG1, Accession NM_015548), a gene which plays a role in cross-linking actin to other cytoskeletal proteins, binds to microtubules. Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BPAG1. The function of BPAG1 and

its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM494.CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838) is another VGAM1249 host target gene. CSMD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CSMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSMD1 BINDING SITE, designated SEQ ID:36189, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44614] Another function of VGAM1249 is therefore inhibition of CUB and Sushi Multiple Domains 1 (CSMD1, Accession XM_054838). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSMD1. KIAA1987 (Accession XM_113870) is another VGAM1249 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42501, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44615] Another function of VGAM1249 is therefore inhibition of KIAA1987 (Accession XM_113870). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM_031469) is another VGAM1249 host target gene. SH3BGRL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BGRL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BGRL2 BINDING SITE, designated SEQ ID:25532, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44616] Another function of VGAM1249 is therefore inhibition of SH3 Domain Binding Glutamic Acid-rich Protein Like 2 (SH3BGRL2, Accession NM_031469). Accordingly, utilities

of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BGRL2. LOC123242 (Accession XM_063548) is another VGAM1249 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37247, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44617] Another function of VGAM1249 is therefore inhibition of LOC123242 (Accession XM_063548). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123242. LOC145945 (Accession XM_096908) is another VGAM1249 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145945 BINDING SITE, designated SEQ ID:40638, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44618] Another function of VGAM1249 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC149013 (Accession XM_086398) is another VGAM1249 host target gene. LOC149013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149013 BINDING SITE, designated SEQ ID:38632, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44619] Another function of VGAM1249 is therefore inhibition of LOC149013 (Accession XM_086398). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149013. LOC253001 (Accession XM_171711) is another VGAM1249 host target gene. LOC253001 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46061, to the nucleotide sequence of VGAM1249 RNA, herein designated VGAM RNA, also designated SEQ ID:3960.

[44620] Another function of VGAM1249 is therefore inhibition of LOC253001 (Accession XM_171711). Accordingly, utilities of VGAM1249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253001. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1250 (VGAM1250) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44621] VGAM1250 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1250 was detected is described hereinabove with reference to Figs. 1-8.

[44622] VGAM1250 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Camelpox Virus.

VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44623] VGAM1250 gene encodes a VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1250 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1250 precursor RNA is designated SEQ ID:1236, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1236 is located at position 136377 relative to the genome of Camelpox Virus.

[44624] VGAM1250 precursor RNA folds onto itself, forming VGAM1250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[44625] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1250 folded precursor RNA into VGAM1250 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1250 RNA is designated SEQ ID:3961, and is provided hereinbelow with reference to the sequence listing part.

[44626] VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1250 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44627] VGAM1250 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1250 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1250 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1250 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44628] The complementary binding of VGAM1250 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1250 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1250 host target RNA into VGAM1250 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44629] It is appreciated that VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1250 host target genes. The mRNA of each one of this plurality of VGAM1250 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1250 RNA, herein designated VGAM RNA, and which when bound by VGAM1250 RNA causes inhibition of translation of respective one or more VGAM1250 host target proteins.

[44630] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1250 gene, herein designated VGAM GENE, on one or more VGAM1250 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44631] It is yet further appreciated that a function of VGAM1250 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGAM1250 correlate with, and may be deduced from, the identity of the host target genes which VGAM1250 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44632] Nucleotide sequences of the VGAM1250 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1250 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1250 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1250 are further described hereinbelow with reference to Table 1.

[44633] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1250 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1250 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44634] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1250 gene, herein designated VGAM is inhibition of expression of VGAM1250 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1250 correlate with, and may be deduced from, the identity of the target genes which VGAM1250 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44635] Glutamate Receptor, Ionotropic, N-methyl D-aspartate-like 1A (GRINL1A, Accession XM_045376) is a VGAM1250 host target gene. GRINL1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRINL1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRINL1A BINDING SITE, designated SEQ ID:34444, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44636] A function of VGAM1250 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate-like 1A (GRINL1A, Accession XM_045376), a gene which plays a role in the development and function of the mammalian brain. Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRINL1A. The function of GRINL1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53.FHX (Accession NM_018416) is another VGAM1250 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20462, to the nucleotide sequence of VGAM1250 RNA, herein

designated VGAM RNA, also designated SEQ ID:3961.

[44637] Another function of VGAM1250 is therefore inhibition of FHX (Accession NM_018416). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHX. FLJ13611 (Accession NM_024941) is another VGAM1250 host target gene. FLJ13611 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13611, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13611 BINDING SITE, designated SEQ ID:24486, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44638] Another function of VGAM1250 is therefore inhibition of FLJ13611 (Accession NM_024941). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13611. KIAA0746 (Accession XM_045277) is another VGAM1250 host target gene. KIAA0746 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0746, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0746 BINDING SITE, designated SEQ ID:34416, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44639] Another function of VGAM1250 is therefore inhibition of KIAA0746 (Accession XM_045277). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0746. KIAA1363 (Accession XM_045056) is another VGAM1250 host target gene. KIAA1363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1363 BINDING SITE, designated SEQ ID:34335, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44640] Another function of VGAM1250 is therefore inhibition of KIAA1363 (Accession XM_045056). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1363. LOC220766 (Accession XM_165471) is another VGAM1250 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43655, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44641] Another function of VGAM1250 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC221964 (Accession XM_168342) is another VGAM1250 host target gene. LOC221964 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221964 BINDING SITE, designated SEQ ID:45111, to

the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44642] Another function of VGAM1250 is therefore inhibition of LOC221964 (Accession XM_168342). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221964. LOC92181 (Accession XM_043394) is another VGAM1250 host target gene. LOC92181 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92181 BINDING SITE, designated SEQ ID:33942, to the nucleotide sequence of VGAM1250 RNA, herein designated VGAM RNA, also designated SEQ ID:3961.

[44643] Another function of VGAM1250 is therefore inhibition of LOC92181 (Accession XM_043394). Accordingly, utilities of VGAM1250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92181. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1251 (VGAM1251) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44644] VGAM1251 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1251 was detected is described hereinabove with reference to Figs. 1–8.

[44645] VGAM1251 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Monkeypox Virus. VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44646] VGAM1251 gene encodes a VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1251 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1251 precursor RNA is designated SEQ ID:1237, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1237 is located at position 132303 relative to the genome of Monkeypox Virus.

[44647] VGAM1251 precursor RNA folds onto itself, forming VGAM1251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44648] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1251 folded precursor RNA into VGAM1251 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1251 RNA is designated SEQ ID:3962, and is provided hereinbelow with reference to the sequence listing part.

[44649] VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1251 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1251 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44650] VGAM1251 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1251 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1251 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44651] The complementary binding of VGAM1251 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1251 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1251 host target RNA into VGAM1251 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44652] It is appreciated that VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1251 host target genes. The mRNA of each one of this plurality of VGAM1251 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1251 RNA, herein designated VGAM RNA, and which when bound by VGAM1251 RNA causes inhibition of translation of respective one or more VGAM1251 host target proteins.

[44653] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1251 gene, herein designated VGAM GENE, on one or more VGAM1251 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44654] It is yet further appreciated that a function of VGAM1251 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGAM1251 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1251 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44655] Nucleotide sequences of the VGAM1251 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1251 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1251 are further described hereinbelow with reference to Table 1.

[44656] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1251 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1251 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44657] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1251 gene, herein designated VGAM is inhibition of expression of VGAM1251 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1251 correlate with, and may be deduced from, the identity of the target genes which VGAM1251

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44658] Dmx-like 1 (DMXL1, Accession NM_005509) is a VGAM1251 host target gene. DMXL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMXL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMXL1 BINDING SITE, designated SEQ ID:12024, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44659] A function of VGAM1251 is therefore inhibition of Dmx-like 1 (DMXL1, Accession NM_005509). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMXL1. Human T-cell Leukemia Virus Enhancer Factor (HTLF, Accession NM_002158) is another VGAM1251 host target gene. HTLF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTLF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of HTLF BINDING SITE, designated SEQ ID:7933, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44660] Another function of VGAM1251 is therefore inhibition of Human T-cell Leukemia Virus Enhancer Factor (HTLF, Accession NM_002158). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTLF. Splicing Factor, Arginine/serine-rich 2, Interacting Protein (SFRS2IP, Accession NM_004719) is another VGAM1251 host target gene. SFRS2IP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SFRS2IP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS2IP BINDING SITE, designated SEQ ID:11086, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44661] Another function of VGAM1251 is therefore inhibition of Splicing Factor, Arginine/serine-rich 2, Interacting Protein (SFRS2IP, Accession NM_004719), a gene which plays an

essential role in pre-mRNA splicing. Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS2IP. The function of SFRS2IP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM700. Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Accession NM_007256) is another VGAM1251 host target gene. SLC21A9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A9 BINDING SITE, designated SEQ ID:14129, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44662] Another function of VGAM1251 is therefore inhibition of Solute Carrier Family 21 (organic anion transporter), Member 9 (SLC21A9, Accession NM_007256), a gene which is Moderately similar to SLC21A2 prostaglandin transporter. Accordingly, utilities of VGAM1251 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A9. The function of SLC21A9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894. V-akt Murine Thymoma Viral Oncogene Homolog 3 (protein kinase B, gamma) (AKT3, Accession NM_005465) is another VGAM1251 host target gene. AKT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT3 BINDING SITE, designated SEQ ID:11960, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44663] Another function of VGAM1251 is therefore inhibition of V-akt Murine Thymoma Viral Oncogene Homolog 3 (protein kinase B, gamma) (AKT3, Accession NM_005465). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT3. Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476) is another

VGAM1251 host target gene. BTN2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A1 BINDING SITE, designated SEQ ID:27805, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44664] Another function of VGAM1251 is therefore inhibition of Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A1. Chromobox Homolog 6 (CBX6, Accession NM_014292) is another VGAM1251 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15581, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3962.

[44665] Another function of VGAM1251 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM_014292). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. DCOHM (Accession NM_032151) is another VGAM1251 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25851, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44666] Another function of VGAM1251 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. FLJ22009 (Accession XM_015700) is another VGAM1251 host target gene. FLJ22009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22009 BINDING SITE, designated SEQ ID:30246, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44667] Another function of VGAM1251 is therefore inhibition of FLJ22009 (Accession XM_015700). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22009. KIAA0193 (Accession NM_014766) is another VGAM1251 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16547, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44668] Another function of VGAM1251 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities

of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. KIAA1364 (Accession XM_032997) is another VGAM1251 host target gene. KIAA1364 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1364 BINDING SITE, designated SEQ ID:31814, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44669] Another function of VGAM1251 is therefore inhibition of KIAA1364 (Accession XM_032997). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1364. Netrin 4 (NTN4, Accession XM_031896) is another VGAM1251 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTN4 BIND-

ING SITE, designated SEQ ID:31509, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44670] Another function of VGAM1251 is therefore inhibition of Netrin 4 (NTN4, Accession XM_031896). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. PRO0943 (Accession NM_018568) is another VGAM1251 host target gene. PRO0943 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0943 BINDING SITE, designated SEQ ID:20650, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44671] Another function of VGAM1251 is therefore inhibition of PRO0943 (Accession NM_018568). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0943. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792) is an-

other VGAM1251 host target gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPNS1 BINDING SITE, designated SEQ ID:28060, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44672] Another function of VGAM1251 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. LOC147632 (Accession NM_138478) is another VGAM1251 host target gene. LOC147632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147632 BINDING SITE, designated SEQ ID:28825, to the nucleotide sequence of VGAM1251 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3962.

[44673] Another function of VGAM1251 is therefore inhibition of LOC147632 (Accession NM_138478). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147632. LOC152426 (Accession XM_098225) is another VGAM1251 host target gene. LOC152426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152426 BINDING SITE, designated SEQ ID:41501, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44674] Another function of VGAM1251 is therefore inhibition of LOC152426 (Accession XM_098225). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152426. LOC165741 (Accession XM_105272) is another VGAM1251 host target gene. LOC165741 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165741, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165741 BINDING SITE, designated SEQ ID:42193, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44675] Another function of VGAM1251 is therefore inhibition of LOC165741 (Accession XM_105272). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165741. LOC200728 (Accession XM_117267) is another VGAM1251 host target gene. LOC200728 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200728 BINDING SITE, designated SEQ ID:43343, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44676] Another function of VGAM1251 is therefore inhibition of LOC200728 (Accession XM_117267). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC200728. LOC51112 (Accession NM_016030) is another VGAM1251 host target gene. LOC51112 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51112 BINDING SITE, designated SEQ ID:18113, to the nucleotide sequence of VGAM1251 RNA, herein designated VGAM RNA, also designated SEQ ID:3962.

[44677] Another function of VGAM1251 is therefore inhibition of LOC51112 (Accession NM_016030). Accordingly, utilities of VGAM1251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51112. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1252 (VGAM1252) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44678] VGAM1252 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1252 was detected is described hereinabove with reference to Figs. 1–8.

[44679] VGAM1252 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44680] VGAM1252 gene encodes a VGAM1252 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1252 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1252 precursor RNA is designated SEQ ID:1238, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1238 is located at position 5977 relative to the genome of Human Adenovirus D.

[44681] VGAM1252 precursor RNA folds onto itself, forming VGAM1252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44682] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1252 folded precursor RNA into VGAM1252 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1252 RNA is designated SEQ ID:3963, and is provided hereinbelow with reference to the sequence listing part.

[44683] VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1252 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44684] VGAM1252 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1252 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1252 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44685] The complementary binding of VGAM1252 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1252 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1252 host target RNA into VGAM1252 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44686] It is appreciated that VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1252 host target genes. The mRNA of each one of this plurality of VGAM1252 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1252 RNA, herein designated VGAM RNA, and which when bound by VGAM1252 RNA causes inhibition of translation of respective one or more VGAM1252 host target proteins.

[44687] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1252 gene, herein designated VGAM GENE, on one or more VGAM1252 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44688] It is yet further appreciated that a function of VGAM1252 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1252 correlate with, and may be deduced from, the identity of the host target genes which VGAM1252 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44689] Nucleotide sequences of the VGAM1252 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1252 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1252 are further described hereinbelow with reference to Table 1.

[44690] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1252 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1252 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44691] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1252 gene, herein designated VGAM is inhibition of expression of VGAM1252 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1252 correlate with, and may be deduced from, the identity of the target genes which VGAM1252 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44692] ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 3 (ABCC3, Accession NM_020038) is a VGAM1252 host target gene. ABCC3 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by ABCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC3 BINDING SITE, designated SEQ ID:21293, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44693] A function of VGAM1252 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 3 (ABCC3, Accession NM_020038), a gene which may act as an inducible transporter in the biliary and intestinal excretion of organic anions. Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC3. The function of ABCC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM505. Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM_000391) is another VGAM1252 host target gene. CLN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLN2,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN2 BINDING SITE, designated SEQ ID:5965, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44694] Another function of VGAM1252 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM_000391). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN2. Inositol 1,4,5-trisphosphate 3-kinase B (ITPKB, Accession NM_002221) is another VGAM1252 host target gene. ITPKB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPKB BINDING SITE, designated SEQ ID:7980, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44695] Another function of VGAM1252 is therefore inhibition of

Inositol 1,4,5-trisphosphate 3-kinase B (ITPKB, Accession NM_002221), a gene which is a type B inositol 1,4,5-trisphosphate 3 kinase. Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPKB. The function of ITPKB has been established by previous studies. Takazawa et al. (1991) isolated a second inositol 1,4,5-trisphosphate 3-kinase cDNA from a human hippocampus cDNA library. Sequencing yielded an open reading frame encoding a 472-amino acid protein with a calculated relative mass of 53,451. The C-terminal part of this enzyme, referred to as 3-kinase-B, namely, residues 187-462, was 68% identical to 3-kinase-A (OMIM Ref. No. 147521) in amino acid sequence. By in situ hybridization, Erneux et al. (1992) mapped the ITPKB gene to 1q41-q43.

[44696] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44697] Erneux, C.; Roeckel, N.; Takazawa, K.; Mailleux, P.; Vassart, G.; Mattei, M. G. : Localization of the genes for human inositol 1,4,5-trisphosphate 3-kinase A (ITPKA) and B (ITPKB) to chromosome regions 15q14-q21 and 1q41-q43, respectively, by in situ hybridization. Ge-

nomics 14: 546–547, 1992. ; and

[44698] Takazawa, K.; Perret, J.; Dumont, J. E.; Erneux, C. : Molecular cloning and expression of a new putative inositol 1,4,5–trisphosphate 3–kinase isoenzyme. Biochem. J. 278: 883–886, 1991.

[44699] Further studies establishing the function and utilities of ITPKB are found in John Hopkins OMIM database record ID 147522, and in cited publications numbered 127–128 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP586P0123 (Accession XM_170681) is another VGAM1252 host target gene. DKFZP586P0123 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP586P0123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586P0123 BINDING SITE, designated SEQ ID:45463, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44700] Another function of VGAM1252 is therefore inhibition of DKFZP586P0123 (Accession XM_170681). Accordingly, utilities of VGAM1252 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP586P0123. Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex) (DLAT, Accession XM_041355) is another VGAM1252 host target gene. DLAT BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DLAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLAT BINDING SITE, designated SEQ ID:33503, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44701] Another function of VGAM1252 is therefore inhibition of Dihydrolipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex) (DLAT, Accession XM_041355). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLAT. FLJ10350 (Accession XM_170946) is another VGAM1252 host target gene. FLJ10350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10350, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10350 BINDING SITE, designated SEQ ID:45728, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44702] Another function of VGAM1252 is therefore inhibition of FLJ10350 (Accession XM_170946). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10350. FLJ20337 (Accession NM_017772) is another VGAM1252 host target gene. FLJ20337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20337 BINDING SITE, designated SEQ ID:19391, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44703] Another function of VGAM1252 is therefore inhibition of FLJ20337 (Accession NM_017772). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20337. Histamine Receptor H3 (HRH3, Accession NM_007232) is another VGAM1252 host target gene. HRH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH3 BINDING SITE, designated SEQ ID:14108, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44704] Another function of VGAM1252 is therefore inhibition of Histamine Receptor H3 (HRH3, Accession NM_007232). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH3. KIAA0284 (Accession XM_032235) is another VGAM1252 host target gene. KIAA0284 BINDING SITE1 and KIAA0284 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0284, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0284

BINDING SITE1 and KIAA0284 BINDING SITE2, designated SEQ ID:31617 and SEQ ID:31616 respectively, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44705] Another function of VGAM1252 is therefore inhibition of KIAA0284 (Accession XM_032235). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0284. PP1057 (Accession NM_031285) is another VGAM1252 host target gene. PP1057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1057 BINDING SITE, designated SEQ ID:25310, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44706] Another function of VGAM1252 is therefore inhibition of PP1057 (Accession NM_031285). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1057. Solute Carrier Family 12, (potassium-chloride

transporter) Member 5 (SLC12A5, Accession NM_020708) is another VGAM1252 host target gene. SLC12A5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC12A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A5 BINDING SITE, designated SEQ ID:21853, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44707] Another function of VGAM1252 is therefore inhibition of Solute Carrier Family 12, (potassium-chloride transporter) Member 5 (SLC12A5, Accession NM_020708). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A5. LOC164584 (Accession XM_092883) is another VGAM1252 host target gene. LOC164584 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC164584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164584 BINDING SITE, designated SEQ ID:40157, to

the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44708] Another function of VGAM1252 is therefore inhibition of LOC164584 (Accession XM_092883). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164584. LOC253216 (Accession XM_170765) is another VGAM1252 host target gene. LOC253216 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253216 BINDING SITE, designated SEQ ID:45517, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44709] Another function of VGAM1252 is therefore inhibition of LOC253216 (Accession XM_170765). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253216. LOC90120 (Accession XM_029168) is another VGAM1252 host target gene. LOC90120 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC90120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90120 BINDING SITE, designated SEQ ID:30850, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44710] Another function of VGAM1252 is therefore inhibition of LOC90120 (Accession XM_029168). Accordingly, utilities of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90120. LOC90288 (Accession XM_030669) is another VGAM1252 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31104, to the nucleotide sequence of VGAM1252 RNA, herein designated VGAM RNA, also designated SEQ ID:3963.

[44711] Another function of VGAM1252 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities

of VGAM1252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1253 (VGAM1253) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44712] VGAM1253 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1253 was detected is described hereinabove with reference to Figs. 1–8.

[44713] VGAM1253 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44714] VGAM1253 gene encodes a VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1253 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1253 precursor RNA is designated SEQ ID:1239, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1239 is located at position 8179 relative to the genome of Human Adenovirus D.

- [44715] VGAM1253 precursor RNA folds onto itself, forming VGAM1253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44716] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1253 folded precursor RNA into VGAM1253 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1253 RNA is designated SEQ ID:3964, and

is provided hereinbelow with reference to the sequence listing part.

[44717] VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1253 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[44718] VGAM1253 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1253 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1253 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44719] The complementary binding of VGAM1253 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1253 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1253 host target RNA into VGAM1253 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44720] It is appreciated that VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1253 host target genes. The mRNA of each one of this plurality of VGAM1253 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1253 RNA, herein designated VGAM RNA, and which when bound by VGAM1253 RNA causes inhibition of translation of respective one or more VGAM1253 host target proteins.

[44721] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1253 gene, herein designated VGAM GENE, on one or more VGAM1253 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44722] It is yet further appreciated that a function of VGAM1253 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1253 correlate with, and may be deduced from, the identity of the host target genes which VGAM1253 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44723] Nucleotide sequences of the VGAM1253 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1253 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1253 are further described hereinbelow with reference to Table 1.

[44724] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1253 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1253 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44725] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1253 gene, herein designated VGAM is inhibition of expression of VGAM1253 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1253 correlate with, and may be deduced from, the identity of the target genes which VGAM1253 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44726] Fibrillin 2 (congenital contractural arachnodactyly) (FBN2, Accession NM_001999) is a VGAM1253 host target gene. FBN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBN2 BINDING SITE, designated SEQ ID:7726, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44727] A function of VGAM1253 is therefore inhibition of Fibrillin 2 (congenital contractural arachnodactyly) (FBN2, Accession NM_001999), a gene which structural component of connective tissue microfibrils that binds calcium. fibrillin-2-containing microfibrils regulate the early process of elastic fiber assembly. Accordingly, utilities of VGAM1253

include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBN2. The function of FBN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM254. Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM_000527) is another VGAM1253 host target gene. LDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LDLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDLR BINDING SITE, designated SEQ ID:6127, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44728] Another function of VGAM1253 is therefore inhibition of Low Density Lipoprotein Receptor (familial hypercholesterolemia) (LDLR, Accession NM_000527), a gene which also acts as a tumor suppressor. Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDLR. The function of LDLR and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1030.START Domain Containing 5 (STARD5, Accession NM_030574) is another VGAM1253 host target gene. STARD5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by STARD5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STARD5 BINDING SITE, designated SEQ ID:24948, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44729] Another function of VGAM1253 is therefore inhibition of START Domain Containing 5 (STARD5, Accession NM_030574). Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD5. FLJ20308 (Accession XM_039852) is another VGAM1253 host target gene. FLJ20308 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20308 BINDING SITE, designated SEQ ID:33197, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44730] Another function of VGAM1253 is therefore inhibition of FLJ20308 (Accession XM_039852). Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20308. PC4 and SFRS1 Interacting Protein 2 (PSIP2, Accession NM_033222) is another VGAM1253 host target gene. PSIP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PSIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSIP2 BINDING SITE, designated SEQ ID:27068, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44731] Another function of VGAM1253 is therefore inhibition of PC4 and SFRS1 Interacting Protein 2 (PSIP2, Accession NM_033222). Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with PSIP2. LOC163682 (Accession XM_099402) is another VGAM1253 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42091, to the nucleotide sequence of VGAM1253 RNA, herein designated VGAM RNA, also designated SEQ ID:3964.

[44732] Another function of VGAM1253 is therefore inhibition of LOC163682 (Accession XM_099402). Accordingly, utilities of VGAM1253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1254 (VGAM1254) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44733] VGAM1254 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1254 was detected is described hereinabove with reference to Figs. 1–8.

[44734] VGAM1254 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44735] VGAM1254 gene encodes a VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1254 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1254 precursor RNA is designated SEQ ID:1240, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1240 is located at position 8988 relative to the genome of Human Adenovirus D.

[44736] VGAM1254 precursor RNA folds onto itself, forming VGAM1254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44737] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1254 folded precursor RNA into VGAM1254 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1254 RNA is designated SEQ ID:3965, and is provided hereinbelow with reference to the sequence listing part.

[44738] VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1254 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44739] VGAM1254 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1254 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1254 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44740] The complementary binding of VGAM1254 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1254 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1254 host target RNA into VGAM1254 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44741] It is appreciated that VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1254 host target genes. The mRNA of each one of this plurality of VGAM1254 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1254 RNA, herein designated VGAM RNA, and which when bound by VGAM1254 RNA causes inhibition of translation of respective one or more VGAM1254 host target proteins.

[44742] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1254 gene, herein designated VGAM GENE, on one or more VGAM1254 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44743] It is yet further appreciated that a function of VGAM1254 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1254 correlate with, and may be deduced from, the identity of the host target genes which VGAM1254 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44744] Nucleotide sequences of the VGAM1254 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1254 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1254 are further described hereinbelow with reference to Table 1.

[44745] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1254 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1254 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44746] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1254 gene, herein designated VGAM is inhibition of expression of VGAM1254 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1254 correlate with, and may be deduced from, the identity of the target genes which VGAM1254 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44747] EH-domain Containing 2 (EHD2, Accession NM_014601) is a VGAM1254 host target gene. EHD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by EHD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EHD2 BINDING SITE, designated SEQ ID:15964, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44748] A function of VGAM1254 is therefore inhibition of EHD domain Containing 2 (EHD2, Accession NM_014601). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EHD2. Eukaryotic Translation Initiation Factor 2, Subunit 3 Gamma, 52kDa (EIF2S3, Accession NM_001415) is another VGAM1254 host target gene. EIF2S3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2S3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2S3 BINDING SITE, designated SEQ ID:7114, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44749] Another function of VGAM1254 is therefore inhibition of

Eukaryotic Translation Initiation Factor 2, Subunit 3 Gamma, 52kDa (EIF2S3, Accession NM_001415), a gene which functions in the early steps of protein synthesis. Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2S3. The function of EIF2S3 has been established by previous studies. Translation initiation factor eIF-2 is a heterotrimeric GTP-binding protein involved in the recruitment of methionyl-tRNA(i) to the 40 S ribosomal subunit. Gasper et al. (1994) cloned a human cDNA encoding the largest subunit of eIF-2, EIF2G. The EIF2G cDNA encodes a 472-amino acid protein with a molecular mass of 51.8 kD and contains 3 consensus GTP-binding elements. Human EIF2G is highly related to the yeast homolog, GCD11, exhibiting 71% sequence identity and an additional 13% similarity. Genes controlling the functions of spermatogenesis, Spy, and expression of the male-specific minor transplantation antigen H-Y, Hya (OMIM Ref. No. 426000), map to a region of the short arm of the mouse Y chromosome, delta-Sxr(b), that lies between the zinc finger genes Zfy1 and Zfy2 (OMIM Ref. No. 490000) and is deleted in Sxr(b) mutant mice. These Sxr(b) mice arose from an original sex-reversed

mutation, Sxr(a), that carries a duplication of most of the Y chromosome short arm translocated to the telomeric end of the pseudoautosomal region of the Y chromosome. Several genes were mapped to that interval of the mouse Y chromosome and each was found to have a homolog on the X chromosome. Four of them, Zfy1 and Zfy2 (OMIM Ref. No. 490000), Ube1y (OMIM Ref. No. 489000), and Df-fry (OMIM Ref. No. 400005), are expressed specifically in the testis and their X homologs (Zfx, 314980; Ube1x, 314370; Dffrx, 300072) are not transcribed from the inactive X chromosome. A further 2, Smyc (OMIM Ref. No. 426000) and Uty (OMIM Ref. No. 400009), are ubiquitously expressed and their X homologs (Smcx, 314690; Utx, 300128) escape X inactivation. Ehrmann et al. (1998) identified another gene from this region of the mouse Y chromosome. It was found to encode the highly conserved eukaryotic translation initiation factor eIF-2-gamma. In the mouse this gene was found to be ubiquitously expressed, to have an X chromosome homolog that maps close to Dmd (OMIM Ref. No. 300377), and to escape X inactivation. The coding regions of the X and Y genes show 86% nucleotide identity and encode the putative products with 98% amino acid identity. Ehrmann et al.

(1998) found that the human homolog is located on Xp21 and also escapes X inactivation. No evidence of a Y copy of this gene was found in humans, however. In both humans and mice, Ehrmann et al. (1998) identified autosomal retroposons of EIF2G in both humans and mice and an additional retroposon on the X chromosome in some mouse strains. Ark blot analysis of eutherian and metatherian genomic DNA indicated that X-Y homologs are present in all species tested except in simian primates and kangaroo and that retroposons are common to a wide range of mammals. ('Zoo blots' are Southern blots of genomic DNA from multiple species without regard to gender; 'ark blots' are Southern blots used to compare male and female from multiple species.)

[44750] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44751] Ehrmann, I. E.; Ellis, P. S.; Mazeyrat, S.; Duthie, S.; Brockdorff, N.; Mattei, M. G.; Gavin, M. A.; Affara, N. A.; Brown, G. M.; Simpson, E.; Mitchell, M. J.; Scott, D. M. : Characterization of genes encoding translation initiation factor eIF-2-gamma in mouse and human: sex chromosome localization, escape from X-inactivation and evolution. Hum.

Molec. Genet. 7: 1725–1737, 1998. ; and

[44752] Gasper, N. J.; Kinzy, T. G.; Scherer, B. J.; Humbelin, M.; Hershey, J. W. B.; Merrick, W. C. : Translation initiation factor eIF-2: cloning and expression of the human cDNA encoding the.

[44753] Further studies establishing the function and utilities of EIF2S3 are found in John Hopkins OMIM database record ID 300161, and in cited publications numbered 11002 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Farnesyltransferase, CAAX Box, Beta (FNTB, Accession NM_002028) is another VGAM1254 host target gene. FNTB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FNTB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FNTB BINDING SITE, designated SEQ ID:7783, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44754] Another function of VGAM1254 is therefore inhibition of Farnesyltransferase, CAAX Box, Beta (FNTB, Accession NM_002028), a gene which transfers farnesyl groups to

proteins. Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FNTB. The function of FNTB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM615. Suppression of Tumorigenicity 7 (ST7, Accession NM_021908) is another VGAM1254 host target gene. ST7 BINDING SITE1 and ST7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7 BINDING SITE1 and ST7 BINDING SITE2, designated SEQ ID:22430 and SEQ ID:20454 respectively, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44755] Another function of VGAM1254 is therefore inhibition of Suppression of Tumorigenicity 7 (ST7, Accession NM_021908), a gene which has a role in regulating cell-environment or cell-cell interactions. Accordingly, utilities of VGAM1254 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with ST7. The function of ST7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107.FLJ14351 (Accession NM_024732) is another VGAM1254 host target gene. FLJ14351 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14351 BINDING SITE, designated SEQ ID:24072, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44756] Another function of VGAM1254 is therefore inhibition of FLJ14351 (Accession NM_024732). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14351. FLJ20154 (Accession XM_053688) is another VGAM1254 host target gene. FLJ20154 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20154 BINDING SITE, designated SEQ ID:36109, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44757] Another function of VGAM1254 is therefore inhibition of FLJ20154 (Accession XM_053688). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20154. FLJ22160 (Accession NM_024585) is another VGAM1254 host target gene. FLJ22160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22160 BINDING SITE, designated SEQ ID:23820, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44758] Another function of VGAM1254 is therefore inhibition of FLJ22160 (Accession NM_024585). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ22160. Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM_004485) is another VGAM1254 host target gene. GNG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNG4 BINDING SITE, designated SEQ ID:10810, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44759] Another function of VGAM1254 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM_004485). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNG4. H2AV (Accession NM_138635) is another VGAM1254 host target gene. H2AV BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by H2AV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AV BINDING SITE, designated SEQ

ID:28911, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44760] Another function of VGAM1254 is therefore inhibition of H2AV (Accession NM_138635). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AV. KIAA1465 (Accession XM_027396) is another VGAM1254 host target gene. KIAA1465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1465 BINDING SITE, designated SEQ ID:30504, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44761] Another function of VGAM1254 is therefore inhibition of KIAA1465 (Accession XM_027396). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1465. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 1 (SLC11A1, Acces-

sion XM_002585) is another VGAM1254 host target gene. SLC11A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A1 BINDING SITE, designated SEQ ID:29902, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44762] Another function of VGAM1254 is therefore inhibition of Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 1 (SLC11A1, Accession XM_002585). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A1. Transducin-like Enhancer of Split 4 (E(sp1) Homolog, Drosophila) (TLE4, Accession XM_042357) is another VGAM1254 host target gene. TLE4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TLE4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TLE4 BINDING SITE, designated SEQ ID:33720, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44763] Another function of VGAM1254 is therefore inhibition of Transducin-like Enhancer of Split 4 (E(sp1) Homolog, *Drosophila*) (TLE4, Accession XM_042357). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLE4. LOC126353 (Accession XM_059034) is another VGAM1254 host target gene. LOC126353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126353 BINDING SITE, designated SEQ ID:36832, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44764] Another function of VGAM1254 is therefore inhibition of LOC126353 (Accession XM_059034). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126353. LOC145725 (Accession XM_085211) is an-

other VGAM1254 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37951, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44765] Another function of VGAM1254 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM1254 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37960, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44766] Another function of VGAM1254 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC146443 (Accession XM_085461) is another VGAM1254 host target gene. LOC146443 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146443 BINDING SITE, designated SEQ ID:38149, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44767] Another function of VGAM1254 is therefore inhibition of LOC146443 (Accession XM_085461). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146443. LOC166983 (Accession XM_106422) is another VGAM1254 host target gene. LOC166983 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC166983, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166983 BINDING SITE, designated SEQ ID:42199, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44768] Another function of VGAM1254 is therefore inhibition of LOC166983 (Accession XM_106422). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166983. LOC196957 (Accession XM_113789) is another VGAM1254 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42432, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44769] Another function of VGAM1254 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196957. LOC196961 (Accession XM_113790) is another VGAM1254 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42441, to the nucleotide sequence of VGAM1254 RNA, herein designated VGAM RNA, also designated SEQ ID:3965.

[44770] Another function of VGAM1254 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM1254 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42459, to the nucleotide sequence of VGAM1254 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3965.

[44771] Another function of VGAM1254 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM1254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1255 (VGAM1255) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44772] VGAM1255 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1255 was detected is described hereinabove with reference to Figs. 1–8.

[44773] VGAM1255 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44774] VGAM1255 gene encodes a VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1255 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1255 precursor RNA is designated SEQ ID:1241, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1241 is located at position 5672 relative to the genome of Human Adenovirus D.

- [44775] VGAM1255 precursor RNA folds onto itself, forming VGAM1255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [44776] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1255 folded precursor RNA into VGAM1255 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1255 RNA is designated SEQ ID:3966, and is provided hereinbelow with reference to the sequence listing part.

[44777] VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1255 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44778] VGAM1255 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1255 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1255 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[44779] The complementary binding of VGAM1255 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1255 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1255 host target RNA into VGAM1255 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44780] It is appreciated that VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1255 host target genes. The mRNA of

each one of this plurality of VGAM1255 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1255 RNA, herein designated VGAM RNA, and which when bound by VGAM1255 RNA causes inhibition of translation of respective one or more VGAM1255 host target proteins.

[44781] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1255 gene, herein designated VGAM GENE, on one or more VGAM1255 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[44782] It is yet further appreciated that a function of VGAM1255 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1255 correlate with, and may be deduced from, the identity of the host target genes which VGAM1255 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44783] Nucleotide sequences of the VGAM1255 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1255 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1255 are further described hereinbelow with reference to Table 1.

[44784] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1255 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1255 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44785] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1255 gene, herein designated VGAM is inhibition of expression of VGAM1255 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1255 correlate with, and may be deduced from, the identity of the target genes which VGAM1255 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44786] Contactin 2 (axonal) (CNTN2, Accession NM_005076) is a VGAM1255 host target gene. CNTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTN2 BINDING SITE, designated SEQ ID:11525, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44787] A function of VGAM1255 is therefore inhibition of Contactin 2 (axonal) (CNTN2, Accession NM_005076), a gene which may play a role in axonal growth and cell adhesion.

Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTN2. The function of CNTN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. FKRP (Accession NM_024301) is another VGAM1255 host target gene. FKRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKRP BINDING SITE, designated SEQ ID:23593, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44788] Another function of VGAM1255 is therefore inhibition of FKRP (Accession NM_024301). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKRP. Hairless Homolog (mouse) (HR, Accession NM_005144) is another VGAM1255 host target gene. HR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HR, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HR BINDING SITE, designated SEQ ID:11618, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44789] Another function of VGAM1255 is therefore inhibition of Hairless Homolog (mouse) (HR, Accession NM_005144). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HR. Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Accession NM_012405) is another VGAM1255 host target gene. ICMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICMT BINDING SITE, designated SEQ ID:14781, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44790] Another function of VGAM1255 is therefore inhibition of Isoprenylcysteine Carboxyl Methyltransferase (ICMT, Ac-

cession NM_012405). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICMT. Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430) is another VGAM1255 host target gene. MN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MN1 BINDING SITE, designated SEQ ID:8276, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44791] Another function of VGAM1255 is therefore inhibition of Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MN1. Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM_020975) is another VGAM1255 host target gene. RET BINDING SITE1 and RET BINDING SITE2 are HOST TARGET binding sites found in untranslated re-

gions of mRNA encoded by RET, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RET BINDING SITE1 and RET BINDING SITE2, designated SEQ ID:21960 and SEQ ID:21786 respectively, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44792] Another function of VGAM1255 is therefore inhibition of Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM_020975), a gene which transduces signals for cell growth and differentiation. Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RET. The function of RET and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381. Ubiquitin-conjugating Enzyme E2H (UBC8 homolog, yeast) (UBE2H, Accession NM_003344) is another VGAM1255 host target gene. UBE2H BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2H, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2H BINDING SITE, designated SEQ ID:9352, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44793] Another function of VGAM1255 is therefore inhibition of Ubiquitin-conjugating Enzyme E2H (UBC8 homolog, yeast) (UBE2H, Accession NM_003344), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2H. The function of UBE2H and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM811.Centaurin, Gamma 1 (CENTG1, Accession NM_014770) is another VGAM1255 host target gene. CENTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CENTG1 BINDING SITE, designated SEQ ID:16563, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44794] Another function of VGAM1255 is therefore inhibition of Centaurin, Gamma 1 (CENTG1, Accession NM_014770). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG1. FLJ10901 (Accession NM_018265) is another VGAM1255 host target gene. FLJ10901 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10901 BINDING SITE, designated SEQ ID:20232, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44795] Another function of VGAM1255 is therefore inhibition of FLJ10901 (Accession NM_018265). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10901. Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM_032664) is another VGAM1255 host target gene. FUT10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT10 BINDING SITE, designated SEQ ID:26391, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44796] Another function of VGAM1255 is therefore inhibition of Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM_032664). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT10. Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903) is another VGAM1255 host target gene. GABBR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GABBR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of GABBR1 BINDING SITE, designated SEQ ID:22424, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44797] Another function of VGAM1255 is therefore inhibition of Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABBR1. KIAA1399 (Accession XM_046685) is another VGAM1255 host target gene. KIAA1399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1399 BINDING SITE, designated SEQ ID:34798, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44798] Another function of VGAM1255 is therefore inhibition of KIAA1399 (Accession XM_046685). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1399. KIAA1924 (Accession XM_057091) is another VGAM1255 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36481, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44799] Another function of VGAM1255 is therefore inhibition of KIAA1924 (Accession XM_057091). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM_028335) is another VGAM1255 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30689, to the nucleotide sequence of

VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44800] Another function of VGAM1255 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM_028335). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPF8. LOC221935 (Accession XM_166537) is another VGAM1255 host target gene. LOC221935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221935 BINDING SITE, designated SEQ ID:44501, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44801] Another function of VGAM1255 is therefore inhibition of LOC221935 (Accession XM_166537). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221935. LOC245771 (Accession XM_167366) is another VGAM1255 host target gene. LOC245771 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245771 BINDING SITE, designated SEQ ID:44637, to the nucleotide sequence of VGAM1255 RNA, herein designated VGAM RNA, also designated SEQ ID:3966.

[44802] Another function of VGAM1255 is therefore inhibition of LOC245771 (Accession XM_167366). Accordingly, utilities of VGAM1255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245771. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1256 (VGAM1256) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44803] VGAM1256 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1256 was detected is described hereinabove with reference to Figs. 1-8.

[44804] VGAM1256 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44805] VGAM1256 gene encodes a VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1256 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1256 precursor RNA is designated SEQ ID:1242, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1242 is located at position 4027 relative to the genome of Human Adenovirus D.

[44806] VGAM1256 precursor RNA folds onto itself, forming VGAM1256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[44807] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1256 folded precursor RNA into VGAM1256 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1256 RNA is designated SEQ ID:3967, and is provided hereinbelow with reference to the sequence listing part.

[44808] VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1256 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44809] VGAM1256 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1256 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1256 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1256 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44810] The complementary binding of VGAM1256 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1256 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1256 host target RNA into VGAM1256 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44811] It is appreciated that VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1256 host target genes. The mRNA of each one of this plurality of VGAM1256 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1256 RNA, herein designated VGAM RNA, and which when bound by VGAM1256 RNA causes inhibition of translation of respective one or more VGAM1256 host target proteins.

[44812] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1256 gene, herein designated VGAM GENE, on one or more VGAM1256 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44813] It is yet further appreciated that a function of VGAM1256 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1256 correlate with, and may be deduced from, the identity of the host target genes which VGAM1256 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44814] Nucleotide sequences of the VGAM1256 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1256 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1256 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1256 are further described hereinbelow with reference to Table 1.

[44815] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1256 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1256 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44816] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1256 gene, herein designated VGAM is inhibition of expression of VGAM1256 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1256 correlate with, and may be deduced from, the identity of the target genes which VGAM1256 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44817] Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM_022977) is a VGAM1256 host target gene. FACL4 BINDING SITE1 and FACL4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FACL4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL4 BINDING SITE1 and FACL4 BINDING SITE2, designated SEQ ID:23251 and SEQ ID:10761 respectively, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44818] A function of VGAM1256 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM_022977). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL4. Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) (ITGA4, Accession NM_000885) is another VGAM1256 host target gene. ITGA4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ITGA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA4 BINDING SITE, designated SEQ ID:6583, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44819] Another function of VGAM1256 is therefore inhibition of

Integrin, Alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) (ITGA4, Accession NM_000885), a gene which recognizes one or more domains within the alternatively spliced cs-1 and cs-5 regions of fibronectin. Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA4. The function of ITGA4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1096. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326) is another VGAM1256 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14714, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44820] Another function of VGAM1256 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326), a gene which interact

with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of MAPRE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. MHC Class II Transactivator (MHC2TA, Accession NM_000246) is another VGAM1256 host target gene. MHC2TA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MHC2TA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MHC2TA BINDING SITE, designated SEQ ID:5779, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44821] Another function of VGAM1256 is therefore inhibition of MHC Class II Transactivator (MHC2TA, Accession NM_000246). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MHC2TA. Matrix Metallo-

proteinase 15 (membrane-inserted) (MMP15, Accession NM_002428) is another VGAM1256 host target gene. MMP15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMP15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP15 BINDING SITE, designated SEQ ID:8263, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44822] Another function of VGAM1256 is therefore inhibition of Matrix Metalloproteinase 15 (membrane-inserted) (MMP15, Accession NM_002428). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP15. AD-020 (Accession NM_020141) is another VGAM1256 host target gene. AD-020 BINDING SITE1 and AD-020 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AD-020, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of AD-020 BINDING SITE1 and AD-020 BINDING SITE2, designated SEQ ID:21339 and SEQ ID:29869 respectively, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44823] Another function of VGAM1256 is therefore inhibition of AD-020 (Accession NM_020141). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AD-020. KIAA1808 (Accession XM_098260) is another VGAM1256 host target gene. KIAA1808 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1808, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1808 BINDING SITE, designated SEQ ID:41547, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44824] Another function of VGAM1256 is therefore inhibition of KIAA1808 (Accession XM_098260). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1808. KIAA1867 (Accession XM_170675) is another VGAM1256 host target gene. KIAA1867 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1867 BINDING SITE, designated SEQ ID:45454, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44825] Another function of VGAM1256 is therefore inhibition of KIAA1867 (Accession XM_170675). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1867. KIAA1904 (Accession XM_056282) is another VGAM1256 host target gene. KIAA1904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1904 BINDING SITE, designated SEQ ID:36382, to the nucleotide sequence of VGAM1256 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3967.

[44826] Another function of VGAM1256 is therefore inhibition of KIAA1904 (Accession XM_056282). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1904. MGC4796 (Accession XM_029031) is another VGAM1256 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30828, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44827] Another function of VGAM1256 is therefore inhibition of MGC4796 (Accession XM_029031). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM_012454) is another VGAM1256 host target gene. TIAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by TIAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAM2 BINDING SITE, designated SEQ ID:14823, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44828] Another function of VGAM1256 is therefore inhibition of T-cell Lymphoma Invasion and Metastasis 2 (TIAM2, Accession NM_012454). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAM2. TSPEAR (Accession NM_144991) is another VGAM1256 host target gene. TSPEAR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSPEAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSPEAR BINDING SITE, designated SEQ ID:29597, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44829] Another function of VGAM1256 is therefore inhibition of

TSPEAR (Accession NM_144991). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSPEAR. LOC158310 (Accession XM_098919) is another VGAM1256 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41943, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44830] Another function of VGAM1256 is therefore inhibition of LOC158310 (Accession XM_098919). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. LOC199990 (Accession XM_114083) is another VGAM1256 host target gene. LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42683, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44831] Another function of VGAM1256 is therefore inhibition of LOC199990 (Accession XM_114083). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. LOC220143 (Accession XM_168046) is another VGAM1256 host target gene. LOC220143 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220143 BINDING SITE, designated SEQ ID:44954, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44832] Another function of VGAM1256 is therefore inhibition of LOC220143 (Accession XM_168046). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220143. LOC90249 (Accession XM_030300) is an-

other VGAM1256 host target gene. LOC90249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90249 BINDING SITE, designated SEQ ID:31011, to the nucleotide sequence of VGAM1256 RNA, herein designated VGAM RNA, also designated SEQ ID:3967.

[44833] Another function of VGAM1256 is therefore inhibition of LOC90249 (Accession XM_030300). Accordingly, utilities of VGAM1256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1257 (VGAM1257) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44834] VGAM1257 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1257 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[44835] VGAM1257 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44836] VGAM1257 gene encodes a VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1257 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1257 precursor RNA is designated SEQ ID:1243, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1243 is located at position 39908 relative to the genome of Yaba-like Disease Virus.

[44837] VGAM1257 precursor RNA folds onto itself, forming VGAM1257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44838] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1257 folded precursor RNA into VGAM1257 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1257 RNA is designated SEQ ID:3968, and is provided hereinbelow with reference to the sequence listing part.

[44839] VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1257 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44840] VGAM1257 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1257 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1257 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1257 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44841] The complementary binding of VGAM1257 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1257 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1257 host target RNA into VGAM1257 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44842] It is appreciated that VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1257 host target genes. The mRNA of each one of this plurality of VGAM1257 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1257 RNA, herein designated VGAM RNA, and which when bound by VGAM1257 RNA causes inhibition of translation of respective one or more VGAM1257 host target proteins.

[44843] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1257 gene, herein designated VGAM GENE, on one or more VGAM1257 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44844] It is yet further appreciated that a function of VGAM1257 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1257 correlate with, and may be deduced from, the identity of the host target genes which VGAM1257 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44845] Nucleotide sequences of the VGAM1257 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1257 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1257 are further described hereinbelow with reference to Table 1.

[44846] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1257 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1257 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44847] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1257 gene, herein designated VGAM is inhibition of expression of VGAM1257 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1257 correlate with, and may be deduced from, the identity of the target genes which VGAM1257 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44848] ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164) is a VGAM1257 host target gene. ABCD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCD2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD2 BINDING SITE, designated SEQ ID:11656, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44849] A function of VGAM1257 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164), a gene which probable transporter. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD2. The function of ABCD2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229.ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702) is another VGAM1257 host target gene. ATP1A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1A2 BINDING SITE, designated SEQ

ID:6369, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44850] Another function of VGAM1257 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1A2. Endothelin Receptor Type A (EDNRA, Accession XM_034331) is another VGAM1257 host target gene. EDNRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EDNRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDNRA BINDING SITE, designated SEQ ID:32061, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44851] Another function of VGAM1257 is therefore inhibition of Endothelin Receptor Type A (EDNRA, Accession XM_034331), a gene which binds endothelins, and induces intracellular calcium flux and arachidonic acid ac-

cumulation. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDNRA. The function of EDNRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM441. Myeloid Cell Leukemia Sequence 1

(BCL2-related) (MCL1, Accession NM_021960) is another VGAM1257 host target gene. MCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCL1 BINDING SITE, designated SEQ ID:22488, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44852] Another function of VGAM1257 is therefore inhibition of Myeloid Cell Leukemia Sequence 1 (BCL2-related) (MCL1, Accession NM_021960), a gene which involved in programming of differentiation and concomitant maintenance of viability. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCL1. The function of MCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1083. Transcription Elongation Factor A (SII), 1 (TCEA1, Accession XM_087370) is another VGAM1257 host target gene. TCEA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCEA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCEA1 BINDING SITE, designated SEQ ID:39204, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44853] Another function of VGAM1257 is therefore inhibition of Transcription Elongation Factor A (SII), 1 (TCEA1, Acces-

sion XM_087370), a gene which helps RNA polymerase II to transcribe past blockages. Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCEA1. The function of TCEA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM211.MGC2376 (Accession NM_023930) is another VGAM1257 host target gene. MGC2376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2376 BINDING SITE, designated SEQ ID:23413, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44854] Another function of VGAM1257 is therefore inhibition of MGC2376 (Accession NM_023930). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2376. MIG2 (Accession XM_051693) is another VGAM1257 host target gene. MIG2 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by MIG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG2 BINDING SITE, designated SEQ ID:35862, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44855] Another function of VGAM1257 is therefore inhibition of MIG2 (Accession XM_051693). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG2. Zinc Finger Protein 387 (ZNF387, Accession NM_014682) is another VGAM1257 host target gene. ZNF387 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF387 BINDING SITE, designated SEQ ID:16179, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44856] Another function of VGAM1257 is therefore inhibition of

Zinc Finger Protein 387 (ZNF387, Accession NM_014682). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF387. LOC151473 (Accession XM_087215) is another VGAM1257 host target gene. LOC151473 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151473, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151473 BINDING SITE, designated SEQ ID:39123, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44857] Another function of VGAM1257 is therefore inhibition of LOC151473 (Accession XM_087215). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151473. LOC151521 (Accession XM_098076) is another VGAM1257 host target gene. LOC151521 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151521, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151521 BINDING SITE, designated SEQ ID:41365, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44858] Another function of VGAM1257 is therefore inhibition of LOC151521 (Accession XM_098076). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151521. LOC197131 (Accession XM_113823) is another VGAM1257 host target gene. LOC197131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197131 BINDING SITE, designated SEQ ID:42448, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44859] Another function of VGAM1257 is therefore inhibition of LOC197131 (Accession XM_113823). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC197131. LOC254973 (Accession XM_172751) is another VGAM1257 host target gene. LOC254973 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254973, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254973 BINDING SITE, designated SEQ ID:46078, to the nucleotide sequence of VGAM1257 RNA, herein designated VGAM RNA, also designated SEQ ID:3968.

[44860] Another function of VGAM1257 is therefore inhibition of LOC254973 (Accession XM_172751). Accordingly, utilities of VGAM1257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254973. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1258 (VGAM1258) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44861] VGAM1258 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1258 was detected is described hereinabove with reference to Figs. 1–8.

[44862] VGAM1258 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44863] VGAM1258 gene encodes a VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1258 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1258 precursor RNA is designated SEQ ID:1244, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1244 is located at position 40891 relative to the genome of Yaba-like Disease Virus.

[44864] VGAM1258 precursor RNA folds onto itself, forming VGAM1258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44865] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1258 folded precursor RNA into VGAM1258 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1258 RNA is designated SEQ ID:3969, and is provided hereinbelow with reference to the sequence listing part.

[44866] VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1258 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44867] VGAM1258 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1258 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1258 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[44868] The complementary binding of VGAM1258 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1258 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1258 host target RNA into VGAM1258 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44869] It is appreciated that VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1258 host target genes. The mRNA of each one of this plurality of VGAM1258 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1258 RNA, herein designated VGAM RNA, and which when bound by VGAM1258 RNA causes inhibition of translation of respective one or more VGAM1258 host target proteins.

[44870] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1258 gene, herein designated VGAM GENE, on one or more VGAM1258 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44871] It is yet further appreciated that a function of VGAM1258 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1258 correlate with, and may be deduced from, the identity of the host target genes which VGAM1258 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44872] Nucleotide sequences of the VGAM1258 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1258 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1258 are further described hereinbelow with reference to Table 1.

[44873] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1258 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1258 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44874] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1258 gene, herein designated VGAM is inhibition of expression of VGAM1258 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1258 correlate with, and may be deduced from, the identity of the target genes which VGAM1258 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44875] Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Alpha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944) is a VGAM1258 host target gene. PPP3CA BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by PPP3CA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP3CA BINDING SITE, designated SEQ ID:6644, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44876] A function of VGAM1258 is therefore inhibition of Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Alpha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944), a gene which is the catalytic subunit of calcium-dependent, calmodulin-stimulated protein phosphatase. Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP3CA. The function of PPP3CA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497.KIAA0471 (Accession NM_014857) is another VGAM1258 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16914, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44877] Another function of VGAM1258 is therefore inhibition of KIAA0471 (Accession NM_014857). Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. KIAA1594 (Accession XM_050754) is another VGAM1258 host target gene. KIAA1594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1594 BINDING SITE, designated SEQ ID:35673, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44878] Another function of VGAM1258 is therefore inhibition of KIAA1594 (Accession XM_050754). Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1594. Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117) is another VGAM1258 host target gene. KLHL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL4 BINDING SITE, designated SEQ ID:21194, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44879] Another function of VGAM1258 is therefore inhibition of Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117). Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL4. LOC219401 (Accession XM_166706) is another VGAM1258 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, desig-

nated SEQ ID:44588, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44880] Another function of VGAM1258 is therefore inhibition of LOC219401 (Accession XM_166706). Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC219686 (Accession XM_165544) is another VGAM1258 host target gene. LOC219686 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219686 BINDING SITE, designated SEQ ID:43677, to the nucleotide sequence of VGAM1258 RNA, herein designated VGAM RNA, also designated SEQ ID:3969.

[44881] Another function of VGAM1258 is therefore inhibition of LOC219686 (Accession XM_165544). Accordingly, utilities of VGAM1258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219686. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1259 (VGAM1259) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44882] VGAM1259 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1259 was detected is described hereinabove with reference to Figs. 1–8.

[44883] VGAM1259 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant Reversion Virus. VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44884] VGAM1259 gene encodes a VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1259 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1259 precursor RNA is designated SEQ ID:1245, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1245 is located at position 4609 relative to the

genome of Blackcurrant Reversion Virus.

[44885] VGAM1259 precursor RNA folds onto itself, forming VGAM1259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44886] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1259 folded precursor RNA into VGAM1259 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1259 RNA is designated SEQ ID:3970, and is provided hereinbelow with reference to the sequence listing part.

[44887] VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1259 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[44888] VGAM1259 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1259 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1259 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44889] The complementary binding of VGAM1259 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1259 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1259 host target RNA into VGAM1259 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44890] It is appreciated that VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1259 host target genes. The mRNA of each one of this plurality of VGAM1259 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1259 RNA, herein designated VGAM RNA, and which when bound by VGAM1259 RNA causes inhibition of translation of respective one or more VGAM1259 host target proteins.

[44891] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1259 gene, herein designated VGAM GENE, on one or more VGAM1259 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44892] It is yet further appreciated that a function of VGAM1259 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of viral infection by Blackcurrant Reversion Virus. Specific functions, and accordingly utilities, of

VGAM1259 correlate with, and may be deduced from, the identity of the host target genes which VGAM1259 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44893] Nucleotide sequences of the VGAM1259 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1259 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1259 are further described hereinbelow with reference to Table 1.

[44894] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1259 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1259 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44895] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1259 gene, herein designated VGAM is inhibition of expression of VGAM1259 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1259 correlate with, and may be deduced

from, the identity of the target genes which VGAM1259 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44896] ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916) is a VGAM1259 host target gene. ATP8A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP8A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8A2 BINDING SITE, designated SEQ ID:44915, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44897] A function of VGAM1259 is therefore inhibition of ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8A2. Cleavage and Polyadenylation Specific Factor 6, 68kDa (CPSF6, Accession NM_007007) is another VGAM1259 host target gene. CPSF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by CPSF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPSF6 BINDING SITE, designated SEQ ID:13869, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44898] Another function of VGAM1259 is therefore inhibition of Cleavage and Polyadenylation Specific Factor 6, 68kDa (CPSF6, Accession NM_007007). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPSF6. HIR Histone Cell Cycle Regulation Defective Homolog A (*S. cerevisiae*) (HIRA, Accession NM_003325) is another VGAM1259 host target gene. HIRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIRA BINDING SITE, designated SEQ ID:9325, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44899] Another function of VGAM1259 is therefore inhibition of HIR Histone Cell Cycle Regulation Defective Homolog A (*S. cerevisiae*) (HIRA, Accession NM_003325), a gene which could have a part in mechanisms of transcriptional regulation similar to that played by yeast hir1 and hir2 together. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIRA. The function of HIRA has been established by previous studies. The human TUPLE1 gene encodes a putative transcription regulator with a sequence similar to that of the yeast TUP1 gene (Halford et al., 1993). The protein product of the TUPLE1 gene contains WD40 domains, motifs thought to be involved in protein-protein interactions. Halford et al. (1993) demonstrated that the TUPLE1 gene maps to chromosome 22 and to the shortest region of deletion overlap in a series of over 100 patients with the DiGeorge syndrome (DGS; 188400), velocardiofacial syndrome (VCFS; 192430), or a related disorder. It is expressed in a range of fetal tissues. Halford et al. (1993) cloned the murine Tuple1 gene and showed that it has strong sequence similarity to the human gene. Since TUPLE1 is a candidate gene for DGS through the mechanism of haploinsufficiency and it might

be possible to produce models of this disorder by creating mutations in the mouse gene, Mattei et al. (1994) mapped the gene to mouse chromosome 16 by isotopic in situ hybridization. The experiments were carried out using metaphase spreads from a WMP male mouse in which all of the autosomes, except 19, were in the form of meta-centric Robertsonian translocations. In the human, TUPLE1 is centromeric to COMT (OMIM Ref. No. 116790), which in turn is centromeric to IGLC1 (OMIM Ref. No. 147220); all of these expressed sequences map to mouse chromosome 16. Magnaghi et al. (1998) reported an interaction between HIRA and the transcription factor PAX3 (OMIM Ref. No. 606597). PAX3 haploinsufficiency results in the mouse 'splotch' and human Waardenburg syndrome (see OMIM Ref. No. 193500) phenotypes. Mice homozygous for PAX3 mutations die in utero with a phenocopy of DiGeorge syndrome, or neonatally with neural tube defects. HIRA was also found to interact with core histones. Thus, altered stoichiometry of complexes containing HIRA may be important for the development of structures affected in Waardenburg syndrome and DiGeorge syndrome.

[44900] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [44901] Halford, S.; Wilson, D. I.; Daw, S. C. M.; Roberts, C.; Wadey, R.; Kamath, S.; Wickremasinghe, A.; Burn, J.; Goodship, J.; Mattei, M.-G.; Moorman, A. F. M.; Scambler, P. J. : Isolation of a gene expressed during early embryogenesis from the region of 22q11 commonly deleted in DiGeorge syndrome. *Hum. Molec. Genet.* 2: 1577–1582, 1993. ; and
- [44902] Magnaghi, P.; Roberts, C.; Lorain, S.; Lipinski, M.; Scambler, P. J. : HIRA, a mammalian homologue of *Saccharomyces cerevisiae* transcriptional co-repressors, interacts with Pax3. *Natur.*
- [44903] Further studies establishing the function and utilities of HIRA are found in John Hopkins OMIM database record ID 600237, and in cited publications numbered 593 and 7692–7698 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LIM Domains Containing 1 (LIMD1, Accession NM_014240) is another VGAM1259 host target gene. LIMD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIMD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of LIMD1 BINDING SITE, designated SEQ ID:15499, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44904] Another function of VGAM1259 is therefore inhibition of LIM Domains Containing 1 (LIMD1, Accession NM_014240). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMD1. NKX3A (Accession NM_006167) is another VGAM1259 host target gene. NKX3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NKX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKX3A BINDING SITE, designated SEQ ID:12829, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44905] Another function of VGAM1259 is therefore inhibition of NKX3A (Accession NM_006167), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1259 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with NKX3A. The function of NKX3A and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM481. Neuregulin 1 (NRG1, Accession NM_013959) is another VGAM1259 host target gene. NRG1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRG1 BINDING SITE, designated SEQ ID:15140, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44906] Another function of VGAM1259 is therefore inhibition of Neuregulin 1 (NRG1, Accession NM_013959), a gene which is essential for neuronal development. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRG1. The function of NRG1 has been established by previous studies. The NEU/ERBB2 protooncogene (OMIM Ref. No. 164870) encodes a molecule that is closely related to epidermal growth factor receptor (EGFR; 131550)

but binds none of the ligands of this receptor. Originally, NEU was identified as a dominant transforming gene in tumors of the peripheral nervous system that were induced by transplacental treatment of rat embryos with N-ethylnitrosourea. The period of susceptibility of NEU to carcinogenesis, i.e., midgestation, correlated with the timing of its expression in the nervous system. The existence of a NEU-specific ligand of endogenous nature activating NEU at a specific developmental stage was suggested. This ligand, known as heregulin (Holmes et al., 1992) or NEU differentiation factor, is a 44-kD glycoprotein that interacts with the NEU/ERBB2 receptor tyrosine kinase to increase its phosphorylation on tyrosine residues. Splice variants of heregulin, referred to as heregulin betas, have been described by Holmes et al. (1992). Animal model experiments lend further support to the function of NRG1. Mice homozygous for disruptions of all NRG1 isoforms, all Ig-NRG1 isoforms, and all cytoplasmic tail-containing isoforms die at embryonic day 10.5 from cardiac defects. In particular, these mice die before significant expression of CRD-NRG1 isoforms, which predominate after midgestation. By histologic analyses, Wolpowitz et al. (2000) found that homozygous CRD-

NRG1-deficient mice had normal neuronal trajectory and outgrowth, but that the projections defasciculated, branched abnormally, and failed to sustain peripheral neuromuscular synaptic development. Newborn mutants had immature skeletal muscle. Schwann cells were generated in the mutants but failed to survive, consistent with the designation of NRG1 as a Schwann cell survival factor. Schwann cells in turn appeared to provide trophic support only after the nerve had entered its target field and had begun synapse formation.

[44907] It is appreciated that the abovementioned animal model for NRG1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[44908] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44909] Holmes, W. E.; Sliwkowski, M. X.; Akita, R. W.; Henzel, W. J.; Lee, J.; Park, J. W.; Yansura, D.; Abadi, N.; Raab, H.; Lewis, G. D.; Shepard, H. M.; Kuang, W.-J.; Wood, W. I.; Goeddel, D. V.; Vandlen, R. L. : Identification of heregulin, a specific activator of p185(erbB2). Science 256: 1205-1210, 1992. ; and

[44910] Wolpowitz, D.; Mason, T. B. A.; Dietrich, P.; Mendelsohn, M.; Talmage, D. A.; Role, L. W. : Cysteine-rich domain isoforms of the neuregulin-1 gene are required for maintenance of periph.

[44911] Further studies establishing the function and utilities of NRG1 are found in John Hopkins OMIM database record ID 142445, and in cited publications numbered 11569-11577, 188 and 11612 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Purinergic Receptor P2Y, G-protein Coupled, 2 (P2RY2, Accession NM_002564) is another VGAM1259 host target gene. P2RY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RY2 BINDING SITE, designated SEQ ID:8413, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44912] Another function of VGAM1259 is therefore inhibition of Purinergic Receptor P2Y, G-protein Coupled, 2 (P2RY2, Accession NM_002564), a gene which mediates cellular

responses to ATP. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RY2. The function of P2RY2 has been established by previous studies. The chloride ion secretory pathway that is defective in cystic fibrosis (OMIM Ref. No. 219700) can be bypassed by an alternative pathway for chloride ion transport that is activated by extracellular nucleotides. Accordingly, the P2 receptor that mediates this effect is a therapeutic target for improving chloride secretion in CF patients. Parr et al. (1994) reported the sequence and functional expression of a cDNA cloned from human airway epithelial cells that encodes a protein with properties of a P2U nucleotide receptor. With a retrovirus system, the human airway clone was stably expressed in 1321N1 astrocytoma cells, a human cell line unresponsive to extracellular nucleotides. Studies of inositol phosphate accumulation and intracellular Ca^{2+} mobilization induced by extracellular nucleotides in 1321N1 cells expressing the receptor identified this clone as the target receptor in human airway epithelia. Parr et al. (1994) also isolated an identical cDNA from human colonic epithelial cells, indicating that this is the same P2U receptor that had been functionally identi-

fied in other human tissues. Expression of the human P2U receptor in 1321N1 cells revealed evidence for autocrine ATP release and stimulation of transduced receptors.

Thus, P2U expression in the cell line was proposed as a useful system for studying autocrine regulatory mechanisms and for screening potential therapeutic drugs. Tai et al. (2000) studied the expression and regulation of the P2UR gene in human granulosa-luteal cells (GLCs) by RT-PCR and Northern blot analysis. Expression of P2UR mRNA was downregulated by human chorionic gonadotropin (CG) in a dose- and time-dependent manner. Treatment with 8-bromo-cAMP and forskolin also attenuated P2UR mRNA levels. The authors concluded that the P2UR mRNA is expressed in human GLCs and that P2UR mRNA is regulated by human CG, cAMP, and forskolin. These findings further supported a potential role of this neurotransmitter receptor in the human ovary.

[44913] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[44914] Parr, C. E.; Sullivan, D. M.; Paradiso, A. M.; Lazarowski, E. R.; Burch, L. H.; Olsen, J. C.; Erb, L.; Weisman, G. A.; Boucher, R. C.; Turner, J. T. : Cloning and expression of a

human P(2U) nucleotide receptor, a target for cystic fibrosis pharmacotherapy. Proc. Nat. Acad. Sci. 91: 3275–3279, 1994. ; and

[44915] Tai, C.-J.; Kang, S. K.; Cheng, K. W.; Choi, K.-C.; Nathwani, P. S.; Leung, P. C. K. : Expression and regulation of P2U–purinergic receptor in human granulosa–luteal cells. J. Clin. End.

[44916] Further studies establishing the function and utilities of P2RY2 are found in John Hopkins OMIM database record ID 600041, and in cited publications numbered 7715–7719 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Piccolo (presynaptic cytomatrix protein) (PCLO, Accession XM_168530) is another VGAM1259 host target gene. PCLO BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCLO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCLO BINDING SITE, designated SEQ ID:45212, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44917] Another function of VGAM1259 is therefore inhibition of

Piccolo (presynaptic cytomatrix protein) (PCLO, Accession XM_168530), a gene which involves in the cycling of synaptic vesicles. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCLO. The function of PCLO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Serine (or cysteine) Proteinase Inhibitor, Clade D (heparin cofactor), Member 1 (SERPIND1, Accession NM_000185) is another VGAM1259 host target gene. SERPIND1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPIND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPIND1 BINDING SITE, designated SEQ ID:5688, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44918] Another function of VGAM1259 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade D (heparin cofactor), Member 1 (SERPIND1, Accession NM_000185). Accordingly, utilities of VGAM1259 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with SERPIND1. Transmembrane, Prostate Androgen Induced RNA (TMEPAI, Accession NM_020182) is another VGAM1259 host target gene. TMEPAI BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TMEPAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEPAI BINDING SITE, designated SEQ ID:21403, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44919] Another function of VGAM1259 is therefore inhibition of Transmembrane, Prostate Androgen Induced RNA (TMEPAI, Accession NM_020182). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEPAI. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662) is another VGAM1259 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19196, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44920] Another function of VGAM1259 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Cadherin-like 26 (CDH26, Accession NM_021810) is another VGAM1259 host target gene. CDH26 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDH26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH26 BINDING SITE, designated SEQ

ID:22369, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44921] Another function of VGAM1259 is therefore inhibition of Cadherin-like 26 (CDH26, Accession NM_021810). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH26. FLJ12587 (Accession NM_022480) is another VGAM1259 host target gene. FLJ12587 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12587, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12587 BINDING SITE, designated SEQ ID:22851, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44922] Another function of VGAM1259 is therefore inhibition of FLJ12587 (Accession NM_022480). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12587. KIAA0759 (Accession XM_041090) is another VGAM1259 host target gene. KIAA0759 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0759 BINDING SITE, designated SEQ ID:33439, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44923] Another function of VGAM1259 is therefore inhibition of KIAA0759 (Accession XM_041090). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0759. MGC4294 (Accession NM_024314) is another VGAM1259 host target gene. MGC4294 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4294 BINDING SITE, designated SEQ ID:23607, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44924] Another function of VGAM1259 is therefore inhibition of

MGC4294 (Accession NM_024314). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4294. SARM (Accession NM_015077) is another VGAM1259 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ ID:17461, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44925] Another function of VGAM1259 is therefore inhibition of SARM (Accession NM_015077). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. LOC146481 (Accession XM_085484) is another VGAM1259 host target gene. LOC146481 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC146481 BINDING SITE, designated SEQ ID:38175, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44926] Another function of VGAM1259 is therefore inhibition of LOC146481 (Accession XM_085484). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146481. LOC152002 (Accession XM_087360) is another VGAM1259 host target gene. LOC152002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152002 BINDING SITE, designated SEQ ID:39196, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44927] Another function of VGAM1259 is therefore inhibition of LOC152002 (Accession XM_087360). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152002. LOC153205 (Accession XM_098322) is an-

other VGAM1259 host target gene. LOC153205 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC153205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153205 BINDING SITE, designated SEQ ID:41579, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44928] Another function of VGAM1259 is therefore inhibition of LOC153205 (Accession XM_098322). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153205. LOC220565 (Accession XM_165417) is another VGAM1259 host target gene. LOC220565 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220565 BINDING SITE, designated SEQ ID:43631, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44929] Another function of VGAM1259 is therefore inhibition of LOC220565 (Accession XM_165417). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220565. LOC221362 (Accession XM_168093) is another VGAM1259 host target gene. LOC221362 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221362 BINDING SITE, designated SEQ ID:45019, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44930] Another function of VGAM1259 is therefore inhibition of LOC221362 (Accession XM_168093). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221362. LOC92078 (Accession XM_042684) is another VGAM1259 host target gene. LOC92078 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92078, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92078 BINDING SITE, designated SEQ ID:33745, to the nucleotide sequence of VGAM1259 RNA, herein designated VGAM RNA, also designated SEQ ID:3970.

[44931] Another function of VGAM1259 is therefore inhibition of LOC92078 (Accession XM_042684). Accordingly, utilities of VGAM1259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92078. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1260 (VGAM1260) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44932] VGAM1260 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1260 was detected is described hereinabove with reference to Figs. 1–8.

[44933] VGAM1260 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant Reversion Virus. VGAM1260 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44934] VGAM1260 gene encodes a VGAM1260 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1260 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1260 precursor RNA is designated SEQ ID:1246, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1246 is located at position 1827 relative to the genome of Blackcurrant Reversion Virus.

[44935] VGAM1260 precursor RNA folds onto itself, forming VGAM1260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44936] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1260 folded precursor RNA into VGAM1260

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM1260 RNA is designated SEQ ID:3971, and is provided hereinbelow with reference to the sequence listing part.

[44937] VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1260 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44938] VGAM1260 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1260 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1260 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44939] The complementary binding of VGAM1260 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1260 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1260 host target RNA into VGAM1260 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[44940] It is appreciated that VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1260 host target genes. The mRNA of each one of this plurality of VGAM1260 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1260 RNA, herein designated VGAM RNA, and which when bound by VGAM1260 RNA causes inhibition of translation of respective one or more VGAM1260 host target proteins.

[44941] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1260 gene, herein designated VGAM GENE, on one or more VGAM1260 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44942] It is yet further appreciated that a function of VGAM1260 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of viral infection by Blackcurrant Reversion Virus. Specific functions, and accordingly utilities, of VGAM1260 correlate with, and may be deduced from, the identity of the host target genes which VGAM1260 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44943] Nucleotide sequences of the VGAM1260 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1260 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1260 are further described hereinbelow with reference to Table 1.

[44944] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1260 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1260 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44945] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1260 gene, herein designated VGAM is inhibition of expression of VGAM1260 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1260 correlate with, and may be deduced from, the identity of the target genes which VGAM1260 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44946] BLAME (Accession NM_020125) is a VGAM1260 host target gene. BLAME BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ ID:21311, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ

ID:3971.

[44947] A function of VGAM1260 is therefore inhibition of BLAME (Accession NM_020125). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326) is another VGAM1260 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14710, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44948] Another function of VGAM1260 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326), a gene which interact with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of

MAPRE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Dynein, Axonemal, Light Polypeptide 4 (DNAL4, Accession NM_005740) is another VGAM1260 host target gene. DNAL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAL4 BINDING SITE, designated SEQ ID:12305, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44949] Another function of VGAM1260 is therefore inhibition of Dynein, Axonemal, Light Polypeptide 4 (DNAL4, Accession NM_005740). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAL4. FLJ10922 (Accession NM_018273) is another VGAM1260 host target gene. FLJ10922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10922, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10922 BINDING SITE, designated SEQ ID:20252, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44950] Another function of VGAM1260 is therefore inhibition of FLJ10922 (Accession NM_018273). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10922. FLJ11286 (Accession NM_018381) is another VGAM1260 host target gene. FLJ11286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11286 BINDING SITE, designated SEQ ID:20413, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44951] Another function of VGAM1260 is therefore inhibition of FLJ11286 (Accession NM_018381). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ11286. KIAA0789 (Accession XM_033113) is another VGAM1260 host target gene. KIAA0789 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0789 BINDING SITE, designated SEQ ID:31844, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44952] Another function of VGAM1260 is therefore inhibition of KIAA0789 (Accession XM_033113). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0789. KIAA1856 (Accession XM_166549) is another VGAM1260 host target gene. KIAA1856 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1856 BINDING SITE, designated SEQ ID:44522, to the

nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44953] Another function of VGAM1260 is therefore inhibition of KIAA1856 (Accession XM_166549). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1856. MGC3248 (Accession NM_032486) is another VGAM1260 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26239, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44954] Another function of VGAM1260 is therefore inhibition of MGC3248 (Accession NM_032486). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. ODZ2 (Accession XM_047995) is another VGAM1260 host target gene. ODZ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by ODZ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ODZ2 BINDING SITE, designated SEQ ID:35098, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44955] Another function of VGAM1260 is therefore inhibition of ODZ2 (Accession XM_047995). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ODZ2. PP1665 (Accession NM_030792) is another VGAM1260 host target gene. PP1665 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1665, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1665 BINDING SITE, designated SEQ ID:25089, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44956] Another function of VGAM1260 is therefore inhibition of PP1665 (Accession NM_030792). Accordingly, utilities of

VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1665. LOC163231 (Accession XM_092094) is another VGAM1260 host target gene. LOC163231 BINDING SITE1 and LOC163231 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC163231, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163231 BINDING SITE1 and LOC163231 BINDING SITE2, designated SEQ ID:40095 and SEQ ID:40096 respectively, to the nucleotide sequence of VGAM1260 RNA, herein designated VGAM RNA, also designated SEQ ID:3971.

[44957] Another function of VGAM1260 is therefore inhibition of LOC163231 (Accession XM_092094). Accordingly, utilities of VGAM1260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163231. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1261 (VGAM1261) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[44958] VGAM1261 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1261 was detected is described hereinabove with reference to Figs. 1–8.

[44959] VGAM1261 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant Reversion Virus. VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44960] VGAM1261 gene encodes a VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1261 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1261 precursor RNA is designated SEQ ID:1247, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1247 is located at position 2798 relative to the genome of Blackcurrant Reversion Virus.

[44961] VGAM1261 precursor RNA folds onto itself, forming VGAM1261 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44962] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1261 folded precursor RNA into VGAM1261 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM1261 RNA is designated SEQ ID:3972, and is provided hereinbelow with reference to the sequence listing part.

[44963] VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1261 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44964] VGAM1261 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1261 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1261 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44965] The complementary binding of VGAM1261 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1261 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1261 host target RNA into VGAM1261 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44966] It is appreciated that VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1261 host target genes. The mRNA of each one of this plurality of VGAM1261 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1261 RNA, herein designated VGAM RNA, and which when bound by VGAM1261 RNA causes inhibition of translation of respective one or more VGAM1261 host target proteins.

[44967] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1261 gene, herein designated VGAM GENE, on one or more VGAM1261 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44968] It is yet further appreciated that a function of VGAM1261 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1261 include diagnosis, prevention and treatment of viral infection by Blackcurrant Reversion Virus. Specific functions, and accordingly utilities, of VGAM1261 correlate with, and may be deduced from, the identity of the host target genes which VGAM1261 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[44969] Nucleotide sequences of the VGAM1261 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1261 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1261 are further described hereinbelow with reference to Table 1.

[44970] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1261 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1261 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44971] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1261 gene, herein designated VGAM is inhibition of expression of VGAM1261 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1261 correlate with, and may be deduced from, the identity of the target genes which VGAM1261 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44972] FLJ21168 (Accession NM_025073) is a VGAM1261 host target gene. FLJ21168 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21168 BINDING SITE, designated SEQ ID:24671, to the nucleotide sequence of VGAM1261 RNA, herein designated VGAM RNA, also designated SEQ ID:3972.

[44973] A function of VGAM1261 is therefore inhibition of FLJ21168 (Accession NM_025073). Accordingly, utilities of VGAM1261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21168. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1262 (VGAM1262) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44974] VGAM1262 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1262 was detected is described hereinabove with reference to Figs. 1–8.

[44975] VGAM1262 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Blackcurrant Reversion Virus. VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44976] VGAM1262 gene encodes a VGAM1262 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1262 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1262 precursor RNA is designated SEQ ID:1248, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1248 is located at position 3891 relative to the genome of Blackcurrant Reversion Virus.

[44977] VGAM1262 precursor RNA folds onto itself, forming VGAM1262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44978] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1262 folded precursor RNA into VGAM1262 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1262 RNA is designated SEQ ID:3973, and is provided hereinbelow with reference to the sequence listing part.

[44979] VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1262 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44980] VGAM1262 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1262 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1262 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[44981] The complementary binding of VGAM1262 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1262 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1262 host target RNA into VGAM1262 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[44982] It is appreciated that VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1262 host target genes. The mRNA of each one of this plurality of VGAM1262 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1262 RNA, herein designated VGAM RNA, and which when bound by VGAM1262 RNA causes inhibition of translation of respective one or more VGAM1262 host target proteins.

[44983] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1262 gene, herein designated VGAM GENE, on one or more VGAM1262 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[44984] It is yet further appreciated that a function of VGAM1262 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1262 include diagnosis, prevention and treatment of viral infection by Blackcurrant Reversion Virus. Specific functions, and accordingly utilities, of VGAM1262 correlate with, and may be deduced from, the identity of the host target genes which VGAM1262 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[44985] Nucleotide sequences of the VGAM1262 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1262 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1262 are further described hereinbelow with reference to Table 1.

[44986] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1262 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1262 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[44987] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1262 gene, herein designated VGAM is inhibition of expression of VGAM1262 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1262 correlate with, and may be deduced from, the identity of the target genes which VGAM1262 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[44988] CD28 Antigen (Tp44) (CD28, Accession NM_006139) is a VGAM1262 host target gene. CD28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD28, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD28 BINDING SITE, designated SEQ ID:12780, to the nucleotide sequence of VGAM1262 RNA, herein designated VGAM RNA, also designated SEQ ID:3973.

[44989] A function of VGAM1262 is therefore inhibition of CD28 Antigen (Tp44) (CD28, Accession NM_006139), a gene which possibly involved in t-cell activation. Accordingly, utilities of VGAM1262 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD28. The function of CD28 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM281.LOC148371 (Accession XM_086164) is another VGAM1262 host target gene. LOC148371 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148371 BINDING SITE, designated SEQ ID:38525, to the nucleotide sequence of

VGAM1262 RNA, herein designated VGAM RNA, also designated SEQ ID:3973.

[44990] Another function of VGAM1262 is therefore inhibition of LOC148371 (Accession XM_086164). Accordingly, utilities of VGAM1262 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148371. LOC221838 (Accession XM_166521) is another VGAM1262 host target gene. LOC221838 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221838 BINDING SITE, designated SEQ ID:44458, to the nucleotide sequence of VGAM1262 RNA, herein designated VGAM RNA, also designated SEQ ID:3973.

[44991] Another function of VGAM1262 is therefore inhibition of LOC221838 (Accession XM_166521). Accordingly, utilities of VGAM1262 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221838. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1263 (VGAM1263) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[44992] VGAM1263 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1263 was detected is described hereinabove with reference to Figs. 1–8.

[44993] VGAM1263 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[44994] VGAM1263 gene encodes a VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1263 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1263 precursor RNA is designated SEQ ID:1249, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1249 is located at position 1764 relative to the genome of Beet Soil-borne Mosaic Virus.

[44995] VGAM1263 precursor RNA folds onto itself, forming VGAM1263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[44996] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1263 folded precursor RNA into VGAM1263 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1263 RNA is designated SEQ ID:3974, and is provided hereinbelow with reference to the sequence listing part.

[44997] VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1263 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1263 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[44998] VGAM1263 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1263 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1263 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[44999] The complementary binding of VGAM1263 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1263 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1263 host target RNA into VGAM1263 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45000] It is appreciated that VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1263 host target genes. The mRNA of each one of this plurality of VGAM1263 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1263 RNA, herein designated VGAM RNA, and which when bound by VGAM1263 RNA causes inhibition of translation of respective one or more VGAM1263 host target proteins.

[45001] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1263 gene, herein designated VGAM GENE, on one or more VGAM1263 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45002] It is yet further appreciated that a function of VGAM1263 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1263 correlate with, and may be deduced from, the

identity of the host target genes which VGAM1263 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45003] Nucleotide sequences of the VGAM1263 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1263 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1263 are further described hereinbelow with reference to Table 1.

[45004] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1263 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1263 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45005] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1263 gene, herein designated VGAM is inhibition of expression of VGAM1263 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1263 correlate with, and may be deduced from, the identity of the target genes which VGAM1263

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45006] Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 8 (SLC7A8, Accession NM_012244) is a VGAM1263 host target gene. SLC7A8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A8 BINDING SITE, designated SEQ ID:14552, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45007] A function of VGAM1263 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 8 (SLC7A8, Accession NM_012244), a gene which helps mediate transport of large and small neutral amino acids. Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A8. The function of SLC7A8 has been established by previous studies. Amino acid transport occurs through several systems, including systems L and γ^+ L. System L mediates high-affinity,

sodium-independent, and trans-stimulated transport of large zwitterionic amino acids. LAT1 (SLC7A5; 600182), y(+)LAT1 (SLC7A7; 603593), and y(+)LAT2 (SLC7A6; 605641) have been identified as light chains of the heterodimeric cell surface antigen 4F2. These subunits induce amino acid transport activity in association with the heavy chain of 4F2 (MDU1; 158070). By searching an EST database with the amino acid sequence of SLC7A5, Borsani et al. (1999) identified an EST corresponding to SLC7A8, a novel gene that encodes a protein sharing significant sequence identity with SLC7A5.

[45008] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45009] Borsani, G.; Bassi, M. T.; Sperandeo, M. P.; De Grandi, A.; Buoninconti, A.; Riboni, M.; Manzoni, M.; Incerti, B.; Pepe, A.; Andria, G.; Ballabio, A.; Sebastio, G. : SLC7A7, encoding a putative permease-related protein, is mutated in patients with lysinuric protein intolerance. *Nature Genet.* 21: 297-301, 1999. ; and

[45010] Pineda, M.; Fernandez, E.; Torrents, D.; Estevez, R.; Lopez, C.; Camps, M.; Lloberas, J.; Zorzano, A.; Palacin, M. : Identification of a membrane protein, LAT-2, that co-

expresses with 4F2.

[45011] Further studies establishing the function and utilities of SLC7A8 are found in John Hopkins OMIM database record ID 604235, and in cited publications numbered 156 and 12054 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ERAP140 (Accession XM_059748) is another VGAM1263 host target gene. ERAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERAP140 BINDING SITE, designated SEQ ID:37088, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45012] Another function of VGAM1263 is therefore inhibition of ERAP140 (Accession XM_059748). Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERAP140. KIAA0865 (Accession XM_028522) is another VGAM1263 host target gene. KIAA0865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0865 BINDING SITE, designated SEQ ID:30711, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45013] Another function of VGAM1263 is therefore inhibition of KIAA0865 (Accession XM_028522). Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0865. KIAA1550 (Accession XM_039393) is another VGAM1263 host target gene. KIAA1550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1550 BINDING SITE, designated SEQ ID:33068, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45014] Another function of VGAM1263 is therefore inhibition of KIAA1550 (Accession XM_039393). Accordingly, utilities

of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1550. KIAA1715 (Accession XM_042834) is another VGAM1263 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33790, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45015] Another function of VGAM1263 is therefore inhibition of KIAA1715 (Accession XM_042834). Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. Neuronal Pentraxin Receptor (NPTXR, Accession NM_014293) is another VGAM1263 host target gene. NPTXR BINDING SITE1 and NPTXR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NPTXR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of NPTXR BINDING SITE1 and NPTXR BINDING SITE2, designated SEQ ID:15582 and SEQ ID:27730 respectively, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45016] Another function of VGAM1263 is therefore inhibition of Neuronal Pentraxin Receptor (NPTXR, Accession NM_014293). Accordingly, utilities of VGAM1263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTXR. LOC253891 (Accession XM_170485) is another VGAM1263 host target gene. LOC253891 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253891 BINDING SITE, designated SEQ ID:45322, to the nucleotide sequence of VGAM1263 RNA, herein designated VGAM RNA, also designated SEQ ID:3974.

[45017] Another function of VGAM1263 is therefore inhibition of LOC253891 (Accession XM_170485). Accordingly, utilities of VGAM1263 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253891. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1264 (VGAM1264) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45018] VGAM1264 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1264 was detected is described hereinabove with reference to Figs. 1–8.

[45019] VGAM1264 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45020] VGAM1264 gene encodes a VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1264 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1264 precursor RNA is desig-

nated SEQ ID:1250, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1250 is located at position 1403 relative to the genome of Beet Soil-borne Mosaic Virus.

- [45021] VGAM1264 precursor RNA folds onto itself, forming VGAM1264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45022] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1264 folded precursor RNA into VGAM1264 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1264 RNA is designated SEQ ID:3975, and is provided hereinbelow with reference to the sequence

listing part.

[45023] VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1264 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45024] VGAM1264 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1264 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1264 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45025] The complementary binding of VGAM1264 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1264 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1264 host target RNA into VGAM1264 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45026] It is appreciated that VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1264 host target genes. The mRNA of each one of this plurality of VGAM1264 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1264 RNA, herein designated VGAM

RNA, and which when bound by VGAM1264 RNA causes inhibition of translation of respective one or more VGAM1264 host target proteins.

[45027] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1264 gene, herein designated VGAM GENE, on one or more VGAM1264 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45028] It is yet further appreciated that a function of VGAM1264 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1264 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1264 correlate with, and may be deduced from, the identity of the host target genes which VGAM1264 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45029] Nucleotide sequences of the VGAM1264 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1264 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1264 are further described hereinbelow with reference to Table 1.

[45030] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1264 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1264 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45031] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1264 gene, herein designated VGAM is

inhibition of expression of VGAM1264 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1264 correlate with, and may be deduced from, the identity of the target genes which VGAM1264 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45032] Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357) is a VGAM1264 host target gene. CASP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP8 BINDING SITE, designated SEQ ID:27209, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45033] A function of VGAM1264 is therefore inhibition of Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM1264 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM145. Interferon Regulatory Factor 1 (IRF1, Accession XM_034862) is another VGAM1264 host target gene. IRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRF1 BINDING SITE, designated SEQ ID:32175, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45034] Another function of VGAM1264 is therefore inhibition of Interferon Regulatory Factor 1 (IRF1, Accession XM_034862), a gene which specifically binds to the upstream regulatory region of type I IFN and IFN-inducible MHC class I genes. Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRF1. The function of IRF1 has been established by previous studies. In the

course of studies of the regulation of type I interferon gene expression (147660, 147640), Miyamoto et al. (1988) identified a nuclear factor, termed interferon regulatory factor-1 (IRF1), that binds to the upstream cis elements of both the interferon- α and the interferon- β genes. It was found that IRF1 functions as a transcriptional activator for the type I IFN genes (Harada et al., 1990). Harada et al. (1989) found that another factor, IRF2 (OMIM Ref. No. 147576), apparently antagonizes the IRF1 effect by competing for the same cis elements. By linkage studies using RFLPs, the IRF1 gene was assigned to 5q23-q31. To assess the possible role of IRF1 in the regulation of cell growth and differentiation, Yamada et al. (1991) generated transgenic mice carrying the human IRF1 gene, the constitutive expression of which was driven at a high level by the juxtaposed human immunoglobulin heavy-chain enhancer. They found that these transgenic mice showed a dramatic reduction in the number of B lymphocytes. Itoh et al. (1991) also mapped IRF1 to chromosome 5 by analysis of mouse-human somatic cell hybrids. Loss of heterozygosity (LOH) at the IRF1 locus occurs frequently in human gastric cancer (OMIM Ref. No. 137215) (Tamura et al., 1996). Nozawa et al. (1998) iden-

tified a point mutation in a human gastric cancer cell line (147575.0001) that changed methionine at codon 8 to leucine and produced an IRF1 protein with reduced transcriptional activity, but unaltered DNA-binding activity. In addition, Harada et al. (1994) had observed alternative splicing of IRF1 mRNA, producing nonfunctional IRF1 protein at high frequencies in patients with myelodysplastic syndrome and acute myelogenous leukemia. Animal model experiments lend further support to the function of IRF1. Ko et al. (2002) noted that *Irf1* $-/-$ mice are deficient in Inos (OMIM Ref. No. 163730), *Il12b* (OMIM Ref. No. 161561), Cd8 (see OMIM Ref. No. 186910)-positive T cells, and natural killer (NK) cells, whereas *Irf2* $-/-$ mice are deficient in NK cells and have dysregulated *Il12b* induction. *Icsbp* (OMIM Ref. No. 601565) $-/-$ mice are deficient in *Il12b*, *Irf2*, and reactive oxygen intermediates (ROIs). The *Irf1*, *Irf2*, and *Icsbp* genes are all inducible by gamma-interferon (*Ifng*; 147570). *Irf1* $-$, *Irf2 $-$, and *Icsbp*-deficient mouse strains have varying susceptibility to different intracellular bacterial and protozoan pathogens. Ko et al. (2002) determined that *Irf1* $-/-$ mice are highly susceptible to fatal liver damage from *Brucella abortus*, the causative agent of brucellosis, which manifests as arthri-*

tis, endocarditis, and meningitis in humans. In contrast, *Irf2* $-/-$ mice are highly resistant to *Brucella*, whereas *Icsbp* $-/-$ mice maintain a plateau of infection similar to that seen in *Il12b* $-/-$ mice. The authors concluded that IL12, reactive nitrogen intermediates, and ROIs are probably crucial immune components in resistance to *Brucella* infection.

[45035] It is appreciated that the abovementioned animal model for IRF1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[45036] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45037] Yamada, G.; Ogawa, M.; Akagi, K.; Miyamoto, H.; Nakano, N.; Itoh, S.; Miyazaki, J.; Nishikawa, S.; Yamamura, K.; Taniguchi, T. : Specific depletion of the B-cell population induced by aberrant expression of human interferon regulatory factor 1 gene in transgenic mice. *Proc. Nat. Acad. Sci.* 88: 532–536, 1991. ; and

[45038] Ko, J.; Gendron-Fitzpatrick, A.; Splitter, G. A. : Susceptibility of IFN regulatory factor-1 and IFN consensus sequence binding protein-deficient mice to brucellosis. *J. Immun.*

168: 2433.

[45039] Further studies establishing the function and utilities of IRF1 are found in John Hopkins OMIM database record ID 147575, and in cited publications numbered 4814, 338 and 3388–3396 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Mitogen–activated Protein Kinase 4 (MAPK4, Accession NM_002747) is another VGAM1264 host target gene. MAPK4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAPK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK4 BINDING SITE, designated SEQ ID:8623, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45040] Another function of VGAM1264 is therefore inhibition of Mitogen–activated Protein Kinase 4 (MAPK4, Accession NM_002747), a gene which phosphorylates microtubule–associated protein–2 may promote entry into the cell cycle. Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical condi–

tions associated with MAPK4. The function of MAPK4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM655. Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM_003889) is another VGAM1264 host target gene. NR1I2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR1I2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR1I2 BINDING SITE, designated SEQ ID:9974, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45041] Another function of VGAM1264 is therefore inhibition of Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM_003889), a gene which binds to a response element in the cyp3a4 gene promoter and activates its expression in response to a wide variety of endobiotics and xenobiotics. Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR1I2. The function of NR1I2 and its association with various diseases and clinical

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM336.TEM6 (Accession NM_022748) is another VGAM1264 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM6 BINDING SITE, designated SEQ ID:22966, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45042] Another function of VGAM1264 is therefore inhibition of TEM6 (Accession NM_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175.Zinc Finger Protein 14 (KOX 6) (ZNF14, Accession NM_021030) is another VGAM1264 host target gene. ZNF14 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by ZNF14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF14 BINDING SITE, designated SEQ ID:22017, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45043] Another function of VGAM1264 is therefore inhibition of Zinc Finger Protein 14 (KOX 6) (ZNF14, Accession NM_021030). Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF14. Chorionic Gonadotropin, Beta Polypeptide 5 (CGB5, Accession NM_033043) is another VGAM1264 host target gene. CGB5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGB5 BINDING SITE, designated SEQ ID:26932, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45044] Another function of VGAM1264 is therefore inhibition of Chorionic Gonadotropin, Beta Polypeptide 5 (CGB5, Accession NM_033043). Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGB5. DKFZp434M0331 (Accession NM_017600) is another VGAM1264 host target gene. DKFZp434M0331 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434M0331, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434M0331 BINDING SITE, designated SEQ ID:19074, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45045] Another function of VGAM1264 is therefore inhibition of DKFZp434M0331 (Accession NM_017600). Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434M0331. DKFZp547I224 (Accession NM_020221) is another VGAM1264 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site

found in the 5' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21481, to the nucleotide sequence of VGAM1264 RNA, herein designated VGAM RNA, also designated SEQ ID:3975.

[45046] Another function of VGAM1264 is therefore inhibition of DKFZp547I224 (Accession NM_020221). Accordingly, utilities of VGAM1264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I224. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1265 (VGAM1265) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45047] VGAM1265 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1265 was detected is described hereinabove with reference to Figs. 1–8.

[45048] VGAM1265 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45049] VGAM1265 gene encodes a VGAM1265 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1265 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1265 precursor RNA is designated SEQ ID:1251, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1251 is located at position 275 relative to the genome of Beet Soil-borne Mosaic Virus.

[45050] VGAM1265 precursor RNA folds onto itself, forming VGAM1265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[45051] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1265 folded precursor RNA into VGAM1265 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1265 RNA is designated SEQ ID:3976, and is provided hereinbelow with reference to the sequence listing part.

[45052] VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1265 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45053] VGAM1265 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1265 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1265 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1265 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45054] The complementary binding of VGAM1265 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1265 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1265 host target RNA into VGAM1265 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45055] It is appreciated that VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1265 host target genes. The mRNA of each one of this plurality of VGAM1265 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1265 RNA, herein designated VGAM RNA, and which when bound by VGAM1265 RNA causes inhibition of translation of respective one or more VGAM1265 host target proteins.

[45056] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1265 gene, herein designated VGAM GENE, on one or more VGAM1265 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45057] It is yet further appreciated that a function of VGAM1265 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1265 correlate with, and may be deduced from, the identity of the host target genes which VGAM1265 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45058] Nucleotide sequences of the VGAM1265 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1265 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1265 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1265 are further described hereinbelow with reference to Table 1.

[45059] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1265 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1265 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45060] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1265 gene, herein designated VGAM is inhibition of expression of VGAM1265 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1265 correlate with, and may be deduced from, the identity of the target genes which VGAM1265 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45061] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 1 (B4GALT1, Accession NM_001497) is a VGAM1265 host target gene. B4GALT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT1 BINDING SITE, designated SEQ ID:7249, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45062] A function of VGAM1265 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 1 (B4GALT1, Accession NM_001497). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT1. Ribosomal Protein L15 (RPL15, Accession NM_002948) is another VGAM1265 host target gene. RPL15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPL15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPL15 BINDING SITE, designated SEQ ID:8862, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45063] Another function of VGAM1265 is therefore inhibition of Ribosomal Protein L15 (RPL15, Accession NM_002948). Accordingly, utilities of VGAM1265 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with RPL15. Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM_002999) is another VGAM1265 host target gene. SDC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC4 BINDING SITE, designated SEQ ID:8895, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45064] Another function of VGAM1265 is therefore inhibition of Syndecan 4 (amphiglycan, ryudocan) (SDC4, Accession NM_002999), a gene which is a cell surface proteoglycan. Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDC4. The function of SDC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM552.AND-1 (Accession NM_007086) is another VGAM1265 host target gene. AND-1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by AND-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AND-1 BINDING SITE, designated SEQ ID:13956, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45065] Another function of VGAM1265 is therefore inhibition of AND-1 (Accession NM_007086). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AND-1. Formyltetrahydrofolate Dehydrogenase (FTHFD, Accession NM_012190) is another VGAM1265 host target gene. FTHFD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FTHFD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FTHFD BINDING SITE, designated SEQ ID:14480, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45066] Another function of VGAM1265 is therefore inhibition of Formyltetrahydrofolate Dehydrogenase (FTHFD, Accession NM_012190). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FTHFD. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6) (GALNT6, Accession NM_007210) is another VGAM1265 host target gene. GALNT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT6 BINDING SITE, designated SEQ ID:14072, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45067] Another function of VGAM1265 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6) (GALNT6, Accession NM_007210). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

GALNT6. KIAA0836 (Accession XM_035390) is another VGAM1265 host target gene. KIAA0836 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0836 BINDING SITE, designated SEQ ID:32250, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45068] Another function of VGAM1265 is therefore inhibition of KIAA0836 (Accession XM_035390). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. KIAA1322 (Accession XM_052626) is another VGAM1265 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36029, to the nucleotide sequence of VGAM1265 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3976.

[45069] Another function of VGAM1265 is therefore inhibition of KIAA1322 (Accession XM_052626). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. Oxysterol Binding Protein-like 5 (OSBPL5, Accession XM_052567) is another VGAM1265 host target gene. OSBPL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL5 BINDING SITE, designated SEQ ID:35992, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45070] Another function of VGAM1265 is therefore inhibition of Oxysterol Binding Protein-like 5 (OSBPL5, Accession XM_052567). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL5. p25 (Accession NM_007030) is another VGAM1265 host target gene. p25 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by p25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of p25 BINDING SITE, designated SEQ ID:13894, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45071] Another function of VGAM1265 is therefore inhibition of p25 (Accession NM_007030). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with p25. RAGB (Accession NM_016656) is another VGAM1265 host target gene. RAGB BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RAGB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAGB BINDING SITE, designated SEQ ID:18780, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45072] Another function of VGAM1265 is therefore inhibition of RAGB (Accession NM_016656). Accordingly, utilities of

VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAGB. LOC148114 (Accession XM_086050) is another VGAM1265 host target gene. LOC148114 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148114 BINDING SITE, designated SEQ ID:38469, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45073] Another function of VGAM1265 is therefore inhibition of LOC148114 (Accession XM_086050). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148114. LOC152641 (Accession XM_087497) is another VGAM1265 host target gene. LOC152641 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC152641 BINDING SITE, designated SEQ ID:39299, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45074] Another function of VGAM1265 is therefore inhibition of LOC152641 (Accession XM_087497). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152641. LOC51696 (Accession NM_016217) is another VGAM1265 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18313, to the nucleotide sequence of VGAM1265 RNA, herein designated VGAM RNA, also designated SEQ ID:3976.

[45075] Another function of VGAM1265 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM1265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1266 (VGAM1266) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45076] VGAM1266 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1266 was detected is described hereinabove with reference to Figs. 1–8.

[45077] VGAM1266 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic Virus. VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45078] VGAM1266 gene encodes a VGAM1266 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1266 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1266 precursor RNA is designated SEQ ID:1252, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1252 is located at position 1065 relative to the

genome of Beet Soil-borne Mosaic Virus.

[45079] VGAM1266 precursor RNA folds onto itself, forming VGAM1266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45080] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1266 folded precursor RNA into VGAM1266 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1266 RNA is designated SEQ ID:3977, and is provided hereinbelow with reference to the sequence listing part.

[45081] VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1266 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[45082] VGAM1266 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1266 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1266 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45083] The complementary binding of VGAM1266 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1266 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1266 host target RNA into VGAM1266 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45084] It is appreciated that VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1266 host target genes. The mRNA of each one of this plurality of VGAM1266 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1266 RNA, herein designated VGAM RNA, and which when bound by VGAM1266 RNA causes inhibition of translation of respective one or more VGAM1266 host target proteins.

[45085] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1266 gene, herein designated VGAM GENE, on one or more VGAM1266 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45086] It is yet further appreciated that a function of VGAM1266 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of

VGAM1266 correlate with, and may be deduced from, the identity of the host target genes which VGAM1266 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45087] Nucleotide sequences of the VGAM1266 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1266 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1266 are further described hereinbelow with reference to Table 1.

[45088] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1266 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1266 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45089] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1266 gene, herein designated VGAM is inhibition of expression of VGAM1266 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1266 correlate with, and may be deduced

from, the identity of the target genes which VGAM1266 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45090] CAPON (Accession XM_034002) is a VGAM1266 host target gene. CAPON BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPON, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPON BINDING SITE, designated SEQ ID:31988, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45091] A function of VGAM1266 is therefore inhibition of CAPON (Accession XM_034002), a gene which binds to neuronal nitric oxide synthase and leads to a decreased access to NMDA receptor-gated calcium influx and a catalytically inactive enzyme. Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPON. The function of CAPON has been established by previous studies. Using the first 377 amino acids of neuronal nitric oxide synthase (nNOS; 163731) as bait in a yeast 2-hybrid screen, Jaffrey

et al. (1998) isolated cDNAs encoding CAPON. CAPON appears to have 2 alternate splice forms, one encoding a 125-amino acid protein and the other encoding a 327-amino acid protein. The 125-amino acid C-terminal fragment of CAPON specifically interacted with nNOS in a 2-hybrid system. The full-length cDNA produces a 503-amino acid protein. CAPON displayed no significant homology to any other class of protein except for an N-terminal 145-amino acid stretch that has residues suggestive of a phosphotyrosine-binding (PTB) domain. Northern blot analysis detected a predominant 7.5-kb transcript only in brain regions, with no expression evident in adrenal, bladder, heart, kidney, lung, and skeletal muscle. Marked regional variations occurred in brain, with highest density in the cerebral cortex and medulla oblongata and lowest levels in the hippocampus. CAPON and nNOS interacted in vivo and in vitro and colocalized in rat brain. CAPON was found to compete with PSD95 (OMIM Ref. No. 602887) for interaction with nNOS, and overexpression of CAPON resulted in a loss of PSD95-nNOS complexes in transfected cells. Jaffrey et al. (1998) concluded that CAPON may influence nNOS by regulating its ability to associate with PSD95-NMDA receptor com-

plexes. They proposed a model of PSD95–nNOS regulation by CAPON in which NMDA receptors are coupled to nNOS through a PSD95 multimer; these interactions are mediated by PDZ domains. In this complex, nNOS is situated close to NMDA receptor–modulated calcium influx. Binding of CAPON results in the reduction of NMDA receptor–PSD95–nNOS complexes, leading to a decreased access to NMDA receptor–gated calcium influx and a catalytically inactive enzyme. Seki et al. (1997) mapped the CAPON gene, which they called KIAA0464, to chromosome 1 by radiation hybrid analysis.

[45092] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45093] Jaffrey, S. R.; Snowman, A. M.; Eliasson, M. J. L.; Cohen, N. A.; Snyder, S. H. : CAPON: a protein associated with neuronal nitric oxide synthase that regulates its interactions with PSD95. *Neuron* 115–124, 1998. ; and

[45094] Seki, N.; Ohira, M.; Nagase, T.; Ishikawa, K.; Miyajima, N.; Nakajima, D.; Nomura, N.; Ohara, O. : Characterization of cDNA clones in size–fractionated cDNA libraries from human brain.

[45095] Further studies establishing the function and utilities of

CAPON are found in John Hopkins OMIM database record ID 605551, and in cited publications numbered 6405 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228) is another VGAM1266 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11723, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45096] Another function of VGAM1266 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its associ-

ation with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Interleukin 18 Receptor 1 (IL18R1, Accession NM_003855) is another VGAM1266 host target gene. IL18R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL18R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL18R1 BINDING SITE, designated SEQ ID:9949, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45097] Another function of VGAM1266 is therefore inhibition of Interleukin 18 Receptor 1 (IL18R1, Accession NM_003855), a gene which is required for dorsal-ventral embryonic polarity and promotes heterophilic cellular adhesion. Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL18R1. The function of IL18R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM37.FLJ10081

(Accession NM_017991) is another VGAM1266 host target gene. FLJ10081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10081 BINDING SITE, designated SEQ ID:19723, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45098] Another function of VGAM1266 is therefore inhibition of FLJ10081 (Accession NM_017991). Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10081. FLJ10511 (Accession NM_018120) is another VGAM1266 host target gene. FLJ10511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10511 BINDING SITE, designated SEQ ID:19899, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM

RNA, also designated SEQ ID:3977.

[45099] Another function of VGAM1266 is therefore inhibition of FLJ10511 (Accession NM_018120). Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10511. KIAA0426 (Accession NM_014724) is another VGAM1266 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16308, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45100] Another function of VGAM1266 is therefore inhibition of KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. LOC150577 (Accession XM_097918) is another VGAM1266 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150577, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41219, to the nucleotide sequence of VGAM1266 RNA, herein designated VGAM RNA, also designated SEQ ID:3977.

[45101] Another function of VGAM1266 is therefore inhibition of LOC150577 (Accession XM_097918). Accordingly, utilities of VGAM1266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150577. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1267 (VGAM1267) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45102] VGAM1267 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1267 was detected is described hereinabove with reference to Figs. 1–8.

[45103] VGAM1267 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Soil-borne Mosaic

Virus. VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45104] VGAM1267 gene encodes a VGAM1267 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1267 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1267 precursor RNA is designated SEQ ID:1253, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1253 is located at position 1249 relative to the genome of Beet Soil-borne Mosaic Virus.

[45105] VGAM1267 precursor RNA folds onto itself, forming VGAM1267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45106] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1267 folded precursor RNA into VGAM1267 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1267 RNA is designated SEQ ID:3978, and is provided hereinbelow with reference to the sequence listing part.

[45107] VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1267 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45108] VGAM1267 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1267 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1267 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45109] The complementary binding of VGAM1267 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1267 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1267 host target RNA into VGAM1267 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45110] It is appreciated that VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1267 host target genes. The mRNA of each one of this plurality of VGAM1267 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1267 RNA, herein designated VGAM RNA, and which when bound by VGAM1267 RNA causes inhibition of translation of respective one or more VGAM1267 host target proteins.

[45111] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1267 gene, herein designated VGAM GENE, on one or more VGAM1267 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45112] It is yet further appreciated that a function of VGAM1267 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1267 include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1267 correlate with, and may be deduced from, the identity of the host target genes which VGAM1267 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45113] Nucleotide sequences of the VGAM1267 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1267 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1267 are further described hereinbelow with reference to Table 1.

[45114] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1267 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1267 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45115] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1267 gene, herein designated VGAM is inhibition of expression of VGAM1267 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1267 correlate with, and may be deduced from, the identity of the target genes which VGAM1267 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45116] Collagen, Type IV, Alpha 6 (COL4A6, Accession NM_001847) is a VGAM1267 host target gene. COL4A6 BINDING SITE1 and COL4A6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A6 BINDING SITE1

and COL4A6 BINDING SITE2, designated SEQ ID:7582 and SEQ ID:27358 respectively, to the nucleotide sequence of VGAM1267 RNA, herein designated VGAM RNA, also designated SEQ ID:3978.

[45117] A function of VGAM1267 is therefore inhibition of Collagen, Type IV, Alpha 6 (COL4A6, Accession NM_001847). Accordingly, utilities of VGAM1267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A6. LOC148756 (Accession XM_097516) is another VGAM1267 host target gene. LOC148756 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148756 BINDING SITE, designated SEQ ID:40901, to the nucleotide sequence of VGAM1267 RNA, herein designated VGAM RNA, also designated SEQ ID:3978.

[45118] Another function of VGAM1267 is therefore inhibition of LOC148756 (Accession XM_097516). Accordingly, utilities of VGAM1267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC148756. LOC151405 (Accession XM_098058) is another VGAM1267 host target gene. LOC151405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151405 BINDING SITE, designated SEQ ID:41337, to the nucleotide sequence of VGAM1267 RNA, herein designated VGAM RNA, also designated SEQ ID:3978.

[45119] Another function of VGAM1267 is therefore inhibition of LOC151405 (Accession XM_098058). Accordingly, utilities of VGAM1267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151405. LOC221061 (Accession XM_167709) is another VGAM1267 host target gene. LOC221061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221061 BINDING SITE, designated SEQ ID:44770, to the nucleotide sequence of VGAM1267 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3978.

[45120] Another function of VGAM1267 is therefore inhibition of LOC221061 (Accession XM_167709). Accordingly, utilities of VGAM1267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221061. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1268 (VGAM1268) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45121] VGAM1268 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1268 was detected is described hereinabove with reference to Figs. 1–8.

[45122] VGAM1268 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Virus A. VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45123] VGAM1268 gene encodes a VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1268 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1268 precursor RNA is designated SEQ ID:1254, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1254 is located at position 6970 relative to the genome of Grapevine Virus A.

- [45124] VGAM1268 precursor RNA folds onto itself, forming VGAM1268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45125] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1268 folded precursor RNA into VGAM1268 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1268 RNA is designated SEQ ID:3979, and is provided hereinbelow with reference to the sequence listing part.

[45126] VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1268 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45127] VGAM1268 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1268 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1268 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45128] The complementary binding of VGAM1268 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1268 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1268 host target RNA into VGAM1268 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45129] It is appreciated that VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1268 host target genes. The mRNA of

each one of this plurality of VGAM1268 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1268 RNA, herein designated VGAM RNA, and which when bound by VGAM1268 RNA causes inhibition of translation of respective one or more VGAM1268 host target proteins.

[45130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1268 gene, herein designated VGAM GENE, on one or more VGAM1268 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[45131] It is yet further appreciated that a function of VGAM1268 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1268 include diagnosis, prevention and treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGAM1268 correlate with, and may be deduced from, the identity of the host target genes which VGAM1268 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45132] Nucleotide sequences of the VGAM1268 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1268 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1268 are further described hereinbelow with reference to Table 1.

[45133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1268 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1268 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45134] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1268 gene, herein designated VGAM is inhibition of expression of VGAM1268 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1268 correlate with, and may be deduced from, the identity of the target genes which VGAM1268 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45135] RNA Binding Motif Protein 3 (RBM3, Accession XM_047024) is a VGAM1268 host target gene. RBM3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RBM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM3 BINDING SITE, designated SEQ ID:34893, to the nucleotide sequence of VGAM1268 RNA, herein designated VGAM RNA, also designated SEQ ID:3979.

[45136] A function of VGAM1268 is therefore inhibition of RNA Binding Motif Protein 3 (RBM3, Accession XM_047024). Accordingly, utilities of VGAM1268 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with RBM3. KIAA0523 (Accession XM_041964) is another VGAM1268 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33643, to the nucleotide sequence of VGAM1268 RNA, herein designated VGAM RNA, also designated SEQ ID:3979.

[45137] Another function of VGAM1268 is therefore inhibition of KIAA0523 (Accession XM_041964). Accordingly, utilities of VGAM1268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 10 (PSMD10, Accession NM_002814) is another VGAM1268 host target gene. PSMD10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSMD10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of PSMD10 BINDING SITE, designated SEQ ID:8679, to the nucleotide sequence of VGAM1268 RNA, herein designated VGAM RNA, also designated SEQ ID:3979.

[45138] Another function of VGAM1268 is therefore inhibition of Proteasome (prosome, macropain) 26S Subunit, Non-ATPase, 10 (PSMD10, Accession NM_002814). Accordingly, utilities of VGAM1268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSMD10. LOC256107 (Accession XM_173003) is another VGAM1268 host target gene. LOC256107 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256107 BINDING SITE, designated SEQ ID:46275, to the nucleotide sequence of VGAM1268 RNA, herein designated VGAM RNA, also designated SEQ ID:3979.

[45139] Another function of VGAM1268 is therefore inhibition of LOC256107 (Accession XM_173003). Accordingly, utilities of VGAM1268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC256107. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1269 (VGAM1269) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45140] VGAM1269 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1269 was detected is described hereinabove with reference to Figs. 1–8.

[45141] VGAM1269 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Virus A. VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45142] VGAM1269 gene encodes a VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1269 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1269 precursor RNA is designated SEQ ID:1255, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1255 is located at position 2009 relative to the genome of Grapevine Virus A.

- [45143] VGAM1269 precursor RNA folds onto itself, forming VGAM1269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45144] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1269 folded precursor RNA into VGAM1269 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1269 RNA is designated SEQ ID:3980, and is provided hereinbelow with reference to the sequence listing part.

[45145] VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1269 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45146] VGAM1269 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1269 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1269 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45147] The complementary binding of VGAM1269 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1269 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1269 host target RNA into VGAM1269 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45148] It is appreciated that VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1269 host target genes. The mRNA of each one of this plurality of VGAM1269 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1269 RNA, herein designated VGAM RNA, and which when bound by VGAM1269 RNA causes

inhibition of translation of respective one or more VGAM1269 host target proteins.

[45149] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1269 gene, herein designated VGAM GENE, on one or more VGAM1269 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45150] It is yet further appreciated that a function of VGAM1269 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1269 include diagnosis, prevention and

treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGAM1269 correlate with, and may be deduced from, the identity of the host target genes which VGAM1269 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45151] Nucleotide sequences of the VGAM1269 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1269 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1269 are further described hereinbelow with reference to Table 1.

[45152] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1269 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1269 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45153] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1269 gene, herein designated VGAM is inhibition of expression of VGAM1269 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1269 correlate with, and may be deduced from, the identity of the target genes which VGAM1269 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45154] DKFZp547J036 (Accession NM_032281) is a VGAM1269 host target gene. DKFZp547J036 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp547J036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547J036 BINDING SITE, designated SEQ ID:26040, to the nucleotide sequence of VGAM1269 RNA, herein designated VGAM RNA, also designated SEQ ID:3980.

[45155] A function of VGAM1269 is therefore inhibition of DKFZp547J036 (Accession NM_032281). Accordingly, utilities of VGAM1269 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547J036. KIAA1337 (Accession XM_052561) is another VGAM1269 host target gene. KIAA1337 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1337, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1337 BINDING SITE, designated SEQ ID:35983, to the nucleotide sequence of VGAM1269 RNA, herein designated VGAM RNA, also designated SEQ ID:3980.

[45156] Another function of VGAM1269 is therefore inhibition of KIAA1337 (Accession XM_052561). Accordingly, utilities of VGAM1269 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1337. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1270 (VGAM1270) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45157] VGAM1270 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1270 was detected is described hereinabove with reference to Figs. 1-8.

[45158] VGAM1270 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Virus A.

VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45159] VGAM1270 gene encodes a VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1270 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1270 precursor RNA is designated SEQ ID:1256, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1256 is located at position 205 relative to the genome of Grapevine Virus A.

[45160] VGAM1270 precursor RNA folds onto itself, forming VGAM1270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45161] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1270 folded precursor RNA into VGAM1270 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1270 RNA is designated SEQ ID:3981, and is provided hereinbelow with reference to the sequence listing part.

[45162] VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1270 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45163] VGAM1270 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1270 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1270 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45164] The complementary binding of VGAM1270 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1270 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1270 host target RNA into VGAM1270 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45165] It is appreciated that VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1270 host target genes. The mRNA of each one of this plurality of VGAM1270 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1270 RNA, herein designated VGAM RNA, and which when bound by VGAM1270 RNA causes inhibition of translation of respective one or more VGAM1270 host target proteins.

[45166] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1270 gene, herein designated VGAM GENE, on one or more VGAM1270 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45167] It is yet further appreciated that a function of VGAM1270 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGAM1270 correlate with, and may be deduced from, the identity of the host target genes which VGAM1270 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45168] Nucleotide sequences of the VGAM1270 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1270 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1270 are further described hereinbelow with reference to Table 1.

[45169] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1270 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1270 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45170] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1270 gene, herein designated VGAM is inhibition of expression of VGAM1270 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1270 correlate with, and may be deduced from, the identity of the target genes which VGAM1270 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45171] Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is a VGAM1270 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15354, to the

nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, also designated SEQ ID:3981.

[45172] A function of VGAM1270 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.DKFZp434O0515 (Accession XM_038277) is another VGAM1270 host target gene. DKFZp434O0515 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434O0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0515 BINDING SITE, designated SEQ ID:32787, to the nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, also designated SEQ ID:3981.

[45173] Another function of VGAM1270 is therefore inhibition of

DKFZp434O0515 (Accession XM_038277). Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0515. LOC148823 (Accession NM_145278) is another VGAM1270 host target gene. LOC148823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148823 BINDING SITE, designated SEQ ID:29794, to the nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, also designated SEQ ID:3981.

[45174] Another function of VGAM1270 is therefore inhibition of LOC148823 (Accession NM_145278). Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148823. LOC152316 (Accession XM_098185) is another VGAM1270 host target gene. LOC152316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152316, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152316 BINDING SITE, designated SEQ ID:41452, to the nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, also designated SEQ ID:3981.

[45175] Another function of VGAM1270 is therefore inhibition of LOC152316 (Accession XM_098185). Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152316. LOC93444 (Accession XM_051455) is another VGAM1270 host target gene. LOC93444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93444 BINDING SITE, designated SEQ ID:35842, to the nucleotide sequence of VGAM1270 RNA, herein designated VGAM RNA, also designated SEQ ID:3981.

[45176] Another function of VGAM1270 is therefore inhibition of LOC93444 (Accession XM_051455). Accordingly, utilities of VGAM1270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC93444. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1271 (VGAM1271) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45177] VGAM1271 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1271 was detected is described hereinabove with reference to Figs. 1–8.

[45178] VGAM1271 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Virus A. VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45179] VGAM1271 gene encodes a VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1271 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1271 precursor RNA is designated SEQ ID:1257, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1257 is located at position 6496 relative to the genome of Grapevine Virus A.

- [45180] VGAM1271 precursor RNA folds onto itself, forming VGAM1271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45181] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1271 folded precursor RNA into VGAM1271 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1271 RNA is designated SEQ ID:3982, and is provided hereinbelow with reference to the sequence listing part.

[45182] VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1271 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45183] VGAM1271 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1271 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1271 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45184] The complementary binding of VGAM1271 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1271 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1271 host target RNA into VGAM1271 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45185] It is appreciated that VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1271 host target genes. The mRNA of each one of this plurality of VGAM1271 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1271 RNA, herein designated VGAM RNA, and which when bound by VGAM1271 RNA causes

inhibition of translation of respective one or more VGAM1271 host target proteins.

[45186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1271 gene, herein designated VGAM GENE, on one or more VGAM1271 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45187] It is yet further appreciated that a function of VGAM1271 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1271 include diagnosis, prevention and

treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGAM1271 correlate with, and may be deduced from, the identity of the host target genes which VGAM1271 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45188] Nucleotide sequences of the VGAM1271 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1271 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1271 are further described hereinbelow with reference to Table 1.

[45189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1271 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1271 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45190] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1271 gene, herein designated VGAM is inhibition of expression of VGAM1271 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1271 correlate with, and may be deduced from, the identity of the target genes which VGAM1271 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45191] Cyclin D-type Binding-protein 1 (CCNDBP1, Accession NM_037370) is a VGAM1271 host target gene. CCNDBP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCNDBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNDBP1 BINDING SITE, designated SEQ ID:27397, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45192] A function of VGAM1271 is therefore inhibition of Cyclin D-type Binding-protein 1 (CCNDBP1, Accession NM_037370). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNDBP1. Phosphotriesterase Related (PTER, Accession NM_030664) is another VGAM1271 host target gene. PTER BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by PTER, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTER BINDING SITE, designated SEQ ID:24998, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45193] Another function of VGAM1271 is therefore inhibition of Phosphotriesterase Related (PTER, Accession NM_030664), a gene which is a phosphotriesterase homology protein. Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTER. The function of PTER and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM713. Soc-2 Suppressor of Clear Homolog (C. elegans) (SHOC2, Accession NM_007373) is another VGAM1271 host target gene. SHOC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SHOC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SHOC2 BINDING SITE, designated SEQ ID:14306, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45194] Another function of VGAM1271 is therefore inhibition of Soc-2 Suppressor of Clear Homolog (*C. elegans*) (SHOC2, Accession NM_007373), a gene which may be a regulator of the let-60 ras pathway. Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHOC2. The function of SHOC2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM464.DKFZP434I116 (Accession NM_015496) is another VGAM1271 host target gene. DKFZP434I116 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434I116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I116 BINDING SITE, designated SEQ ID:17764, to the nucleotide sequence of

VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45195] Another function of VGAM1271 is therefore inhibition of DKFZP434I116 (Accession NM_015496). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I116. FLJ13848 (Accession NM_024771) is another VGAM1271 host target gene. FLJ13848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13848 BINDING SITE, designated SEQ ID:24132, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45196] Another function of VGAM1271 is therefore inhibition of FLJ13848 (Accession NM_024771). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13848. KIAA1257 (Accession XM_031577) is another VGAM1271 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31436, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45197] Another function of VGAM1271 is therefore inhibition of KIAA1257 (Accession XM_031577). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. LOC128989 (Accession XM_059310) is another VGAM1271 host target gene. LOC128989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36945, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45198] Another function of VGAM1271 is therefore inhibition of LOC128989 (Accession XM_059310). Accordingly, utilities

of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128989. LOC146894 (Accession NM_145273) is another VGAM1271 host target gene. LOC146894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146894 BINDING SITE, designated SEQ ID:29783, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45199] Another function of VGAM1271 is therefore inhibition of LOC146894 (Accession NM_145273). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146894. LOC150155 (Accession XM_047977) is another VGAM1271 host target gene. LOC150155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150155 BINDING SITE, designated SEQ ID:35090, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45200] Another function of VGAM1271 is therefore inhibition of LOC150155 (Accession XM_047977). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150155. LOC150383 (Accession XM_086905) is another VGAM1271 host target gene. LOC150383 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150383, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150383 BINDING SITE, designated SEQ ID:38946, to the nucleotide sequence of VGAM1271 RNA, herein designated VGAM RNA, also designated SEQ ID:3982.

[45201] Another function of VGAM1271 is therefore inhibition of LOC150383 (Accession XM_086905). Accordingly, utilities of VGAM1271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150383. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1272 (VGAM1272) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45202] VGAM1272 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1272 was detected is described hereinabove with reference to Figs. 1–8.

[45203] VGAM1272 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Virus A. VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45204] VGAM1272 gene encodes a VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1272 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1272 precursor RNA is designated SEQ ID:1258, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1258 is located at position 2895 relative to the

genome of Grapevine Virus A.

[45205] VGAM1272 precursor RNA folds onto itself, forming VGAM1272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45206] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1272 folded precursor RNA into VGAM1272 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1272 RNA is designated SEQ ID:3983, and is provided hereinbelow with reference to the sequence listing part.

[45207] VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1272 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[45208] VGAM1272 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1272 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1272 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45209] The complementary binding of VGAM1272 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1272 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1272 host target RNA into VGAM1272 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45210] It is appreciated that VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1272 host target genes. The mRNA of each one of this plurality of VGAM1272 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1272 RNA, herein designated VGAM RNA, and which when bound by VGAM1272 RNA causes inhibition of translation of respective one or more VGAM1272 host target proteins.

[45211] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1272 gene, herein designated VGAM GENE, on one or more VGAM1272 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45212] It is yet further appreciated that a function of VGAM1272 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGAM1272 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1272 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45213] Nucleotide sequences of the VGAM1272 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1272 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1272 are further described hereinbelow with reference to Table 1.

[45214] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1272 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1272 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45215] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1272 gene, herein designated VGAM is inhibition of expression of VGAM1272 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1272 correlate with, and may be deduced

from, the identity of the target genes which VGAM1272 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45216] Deiodinase, Iodothyronine, Type I (DIO1, Accession NM_000792) is a VGAM1272 host target gene. DIO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO1 BINDING SITE, designated SEQ ID:6451, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45217] A function of VGAM1272 is therefore inhibition of Deiodinase, Iodothyronine, Type I (DIO1, Accession NM_000792). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO1. High-mobility Group Box 3 (HMGB3, Accession NM_005342) is another VGAM1272 host target gene. HMGB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMGB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMGB3 BINDING SITE, designated SEQ ID:11817, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45218] Another function of VGAM1272 is therefore inhibition of High-mobility Group Box 3 (HMGB3, Accession NM_005342), a gene which plays a fundamental role in DNA replication, nucleosome assembly, and transcription. Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMGB3. The function of HMGB3 has been established by previous studies. One group of high mobility group (HMG) proteins includes the HMG1 (OMIM Ref. No. 163905) and HMG2 (OMIM Ref. No. 163906) proteins, which appear to play a fundamental role in DNA replication, nucleosome assembly, and transcription. By using direct cDNA selection to identify genes located in human chromosome Xq28, Wilke et al. (1997) cloned cDNAs encoding the human homolog of chicken HMG2a. The predicted 199-amino acid human protein shares 97%, 88%, and 86% identity with chicken HMG2a, human HMG1, and human HMG2, respectively. Like the HMG1 and HMG2

proteins, human HMG2A contains 2 HMG box repeats and an acidic C-terminal domain. Northern blot analysis revealed that HMG2A is expressed predominantly in placenta as 1.2- and 1.7-kb mRNAs. Wilke et al. (1997) also identified ESTs corresponding to the mouse HMG2a homolog. Independently, Vaccari et al. (1998) isolated mouse and human cDNAs corresponding to HGM2A, which they called HMG4. They reported that the deduced mouse and human proteins contain 200 amino acids and are 97% identical. Northern blot and RT-PCR analyses suggested that mouse Hmg4 transcripts are much more abundant in embryonic than in adult tissues.

[45219] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45220] Vaccari, T.; Beltrame, M.; Ferrari, S.; Bianchi, M. E. : Hmg4, a new member of the Hmg1/2 gene family. *Genomics* 49: 247-252, 1998. ; and

[45221] Wilke, K.; Wiemann, S.; Gaul, R.; Gong, W.; Poustka, A. : Isolation of human and mouse HMG2a cDNAs: evidence for an HMG2a-specific 3-prime untranslated region. *Gene* 198: 269-274, 1997.

[45222] Further studies establishing the function and utilities of

HMGB3 are found in John Hopkins OMIM database record ID 300193, and in cited publications numbered 11391–11392 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Integrin, Alpha 6 (ITGA6, Accession NM_000210) is another VGAM1272 host target gene. ITGA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA6 BINDING SITE, designated SEQ ID:5703, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45223] Another function of VGAM1272 is therefore inhibition of Integrin, Alpha 6 (ITGA6, Accession NM_000210). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA6. Latent Transforming Growth Factor Beta Binding Protein 2 (LTBP2, Accession NM_000428) is another VGAM1272 host target gene. LTBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LTBP2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTBP2 BINDING SITE, designated SEQ ID:6005, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45224] Another function of VGAM1272 is therefore inhibition of Latent Transforming Growth Factor Beta Binding Protein 2 (LTBP2, Accession NM_000428), a gene which targets latent TGF-beta to the extracellular matrix. Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTBP2. The function of LTBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM476. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155) is another VGAM1272 host target gene. SERPINB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SERPINB9 BINDING SITE, designated SEQ ID:10361, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45225] Another function of VGAM1272 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155), a gene which may be a serpin serine protease inhibitor that interacts with granzyme B (GZMB). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB9. The function of SERPINB9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60. Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM_059257) is another VGAM1272 host target gene. C20orf142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf142 BINDING

SITE, designated SEQ ID:36929, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45226] Another function of VGAM1272 is therefore inhibition of Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM_059257). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf142. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033331) is another VGAM1272 host target gene. CDC14B BINDING SITE1 and CDC14B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDC14B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE1 and CDC14B BINDING SITE2, designated SEQ ID:27160 and SEQ ID:9757 respectively, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45227] Another function of VGAM1272 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*)

(CDC14B, Accession NM_033331). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. Death Associated Transcription Factor 1 (DATF1, Accession NM_080796) is another VGAM1272 host target gene. DATF1 BINDING SITE1 and DATF1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DATF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DATF1 BINDING SITE1 and DATF1 BINDING SITE2, designated SEQ ID:28064 and SEQ ID:15317 respectively, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45228] Another function of VGAM1272 is therefore inhibition of Death Associated Transcription Factor 1 (DATF1, Accession NM_080796). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DATF1. FLJ11011 (Accession NM_018299) is another VGAM1272 host target gene. FLJ11011 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by FLJ11011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11011 BINDING SITE, designated SEQ ID:20291, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45229] Another function of VGAM1272 is therefore inhibition of FLJ11011 (Accession NM_018299). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11011. FLJ31153 (Accession NM_144600) is another VGAM1272 host target gene. FLJ31153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31153 BINDING SITE, designated SEQ ID:29413, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45230] Another function of VGAM1272 is therefore inhibition of FLJ31153 (Accession NM_144600). Accordingly, utilities of

VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31153. HSA250839 (Accession NM_018401) is another VGAM1272 host target gene. HSA250839 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA250839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA250839 BINDING SITE, designated SEQ ID:20438, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45231] Another function of VGAM1272 is therefore inhibition of HSA250839 (Accession NM_018401). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA250839. KIAA0377 (Accession NM_014659) is another VGAM1272 host target gene. KIAA0377 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0377, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0377 BINDING SITE, designated SEQ ID:16103, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45232] Another function of VGAM1272 is therefore inhibition of KIAA0377 (Accession NM_014659). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0377. Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM_004713) is another VGAM1272 host target gene. SDCCAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDCCAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCCAG1 BINDING SITE, designated SEQ ID:11071, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45233] Another function of VGAM1272 is therefore inhibition of Serologically Defined Colon Cancer Antigen 1 (SDCCAG1, Accession NM_004713). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SD-

CCAG1. LOC122330 (Accession XM_074145) is another VGAM1272 host target gene. LOC122330 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122330, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122330 BINDING SITE, designated SEQ ID:37517, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45234] Another function of VGAM1272 is therefore inhibition of LOC122330 (Accession XM_074145). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122330. LOC256401 (Accession XM_171149) is another VGAM1272 host target gene. LOC256401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256401 BINDING SITE, designated SEQ ID:45944, to the nucleotide sequence of VGAM1272 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3983.

[45235] Another function of VGAM1272 is therefore inhibition of LOC256401 (Accession XM_171149). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256401. LOC90719 (Accession XM_033704) is another VGAM1272 host target gene. LOC90719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90719 BINDING SITE, designated SEQ ID:31946, to the nucleotide sequence of VGAM1272 RNA, herein designated VGAM RNA, also designated SEQ ID:3983.

[45236] Another function of VGAM1272 is therefore inhibition of LOC90719 (Accession XM_033704). Accordingly, utilities of VGAM1272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90719. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1273 (VGAM1273) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45237] VGAM1273 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1273 was detected is described hereinabove with reference to Figs. 1–8.

[45238] VGAM1273 gene, herein designated VGAM GENE, is a viral gene contained in the genome of A–2 Plaque Virus. VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45239] VGAM1273 gene encodes a VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1273 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1273 precursor RNA is designated SEQ ID:1259, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1259 is located at position 7172 relative to the genome of A–2 Plaque Virus.

[45240] VGAM1273 precursor RNA folds onto itself, forming

VGAM1273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45241] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1273 folded precursor RNA into VGAM1273 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM1273 RNA is designated SEQ ID:3984, and is provided hereinbelow with reference to the sequence listing part.

[45242] VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1273 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45243] VGAM1273 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1273 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1273 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45244] The complementary binding of VGAM1273 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1273 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1273 host target RNA into VGAM1273 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45245] It is appreciated that VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1273 host target genes. The mRNA of each one of this plurality of VGAM1273 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1273 RNA, herein designated VGAM RNA, and which when bound by VGAM1273 RNA causes inhibition of translation of respective one or more VGAM1273 host target proteins.

[45246] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1273 gene, herein designated VGAM GENE, on one or more VGAM1273 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45247] It is yet further appreciated that a function of VGAM1273 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific functions, and accordingly utilities, of VGAM1273 correlate with, and may be deduced from, the identity of the host target genes which VGAM1273 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[45248] Nucleotide sequences of the VGAM1273 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1273 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1273 are further described hereinbelow with reference to Table 1.

[45249] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1273 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1273 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45250] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1273 gene, herein designated VGAM is inhibition of expression of VGAM1273 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1273 correlate with, and may be deduced from, the identity of the target genes which VGAM1273 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[45251] Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093) is a VGAM1273 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11547, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45252] A function of VGAM1273 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Ac-

cession NM_000782) is another VGAM1273 host target gene. CYP24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP24 BINDING SITE, designated SEQ ID:6430, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45253] Another function of VGAM1273 is therefore inhibition of Cytochrome P450, Subfamily XXIV (vitamin D 24-hydroxylase) (CYP24, Accession NM_000782), a gene which induces the differentiation of promyelocytes into monocytes/macrophages. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP24. The function of CYP24 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1204.DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397) is another VGAM1273 host target gene.

DDX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX6 BINDING SITE, designated SEQ ID:10643, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45254] Another function of VGAM1273 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397), a gene which is putative RNA helicases. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX6. The function of DDX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Galactosamine (N-acetyl)-6-sulfate Sulfatase (Morquio syndrome, mucopolysaccharidosis type IVA) (GALNS, Accession NM_000512) is another VGAM1273 host target gene. GALNS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNS, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNS BINDING SITE, designated SEQ ID:6121, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45255] Another function of VGAM1273 is therefore inhibition of Galactosamine (N-acetyl)-6-sulfate Sulfatase (Morquio syndrome, mucopolysaccharidosis type IVA) (GALNS, Accession NM_000512). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNS. Heterogeneous Nuclear Ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa) (HNRPD, Accession NM_002138) is another VGAM1273 host target gene. HNRPD BINDING SITE1 and HNRPD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HNRPD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPD BINDING SITE1 and HNRPD BINDING SITE2, designated SEQ ID:7914 and SEQ ID:25364 respectively, to the nucleotide sequence of

VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45256] Another function of VGAM1273 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa) (HNRPD, Accession NM_002138). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPD. Src Homology Three (SH3) and Cysteine Rich Domain (STAC, Accession NM_003149) is another VGAM1273 host target gene. STAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAC BINDING SITE, designated SEQ ID:9118, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45257] Another function of VGAM1273 is therefore inhibition of Src Homology Three (SH3) and Cysteine Rich Domain (STAC, Accession NM_003149), a gene which is probably involved in a neuron-specific signal transduction. Accordingly, utilities of VGAM1273 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with STAC. The function of STAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM331. Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM_003316) is another VGAM1273 host target gene. TTC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTC3 BINDING SITE, designated SEQ ID:9316, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45258] Another function of VGAM1273 is therefore inhibition of Tetratricopeptide Repeat Domain 3 (TTC3, Accession NM_003316), a gene which contains tetratricopeptide repeat (TPR) motifs. Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTC3. The function of TTC3 and its association with various diseases and clinical conditions, has been established by previous studies, as

described hereinabove with reference to VGAM699. Angiomotin (AMOT, Accession NM_133265) is another VGAM1273 host target gene. AMOT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOT BINDING SITE, designated SEQ ID:28417, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45259] Another function of VGAM1273 is therefore inhibition of Angiomotin (AMOT, Accession NM_133265). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOT. UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 1 (B3GNT1, Accession NM_006577) is another VGAM1273 host target gene. B3GNT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by B3GNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of B3GNT1 BINDING SITE, designated SEQ ID:13343, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45260] Another function of VGAM1273 is therefore inhibition of UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 1 (B3GNT1, Accession NM_006577). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT1. DKFZp434E1822 (Accession XM_043624) is another VGAM1273 host target gene. DKFZp434E1822 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434E1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434E1822 BINDING SITE, designated SEQ ID:33983, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45261] Another function of VGAM1273 is therefore inhibition of DKFZp434E1822 (Accession XM_043624). Accordingly,

utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434E1822. FLJ20297 (Accession NM_017751) is another VGAM1273 host target gene. FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20297, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE1 and FLJ20297 BINDING SITE2, designated SEQ ID:19359 and SEQ ID:19649 respectively, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45262] Another function of VGAM1273 is therefore inhibition of FLJ20297 (Accession NM_017751). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20297. G2 (Accession XM_039515) is another VGAM1273 host target gene. G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G2 BINDING SITE, designated SEQ ID:33113, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45263] Another function of VGAM1273 is therefore inhibition of G2 (Accession XM_039515). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G2. KIAA0286 (Accession XM_043118) is another VGAM1273 host target gene. KIAA0286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0286 BINDING SITE, designated SEQ ID:33904, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45264] Another function of VGAM1273 is therefore inhibition of KIAA0286 (Accession XM_043118). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0286. Phospholipase A2, Group XII (PLA2G12, Accession NM_030821) is another VGAM1273 host target gene. PLA2G12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G12 BINDING SITE, designated SEQ ID:25150, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45265] Another function of VGAM1273 is therefore inhibition of Phospholipase A2, Group XII (PLA2G12, Accession NM_030821). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G12. SV2B (Accession NM_014848) is another VGAM1273 host target gene. SV2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SV2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SV2B BINDING SITE, designated SEQ ID:16883, to the nu-

cleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45266] Another function of VGAM1273 is therefore inhibition of SV2B (Accession NM_014848). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SV2B. LOC133634 (Accession XM_059664) is another VGAM1273 host target gene. LOC133634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133634 BINDING SITE, designated SEQ ID:37050, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45267] Another function of VGAM1273 is therefore inhibition of LOC133634 (Accession XM_059664). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133634. LOC146146 (Accession XM_085343) is another VGAM1273 host target gene. LOC146146 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC146146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146146 BINDING SITE, designated SEQ ID:38073, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45268] Another function of VGAM1273 is therefore inhibition of LOC146146 (Accession XM_085343). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146146. LOC146452 (Accession XM_085473) is another VGAM1273 host target gene. LOC146452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146452 BINDING SITE, designated SEQ ID:38165, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45269] Another function of VGAM1273 is therefore inhibition of LOC146452 (Accession XM_085473). Accordingly, utilities

of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146452. LOC150630 (Accession XM_097931) is another VGAM1273 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41242, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45270] Another function of VGAM1273 is therefore inhibition of LOC150630 (Accession XM_097931). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. LOC150776 (Accession XM_032542) is another VGAM1273 host target gene. LOC150776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150776 BINDING SITE, designated SEQ ID:31676, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45271] Another function of VGAM1273 is therefore inhibition of LOC150776 (Accession XM_032542). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150776. LOC164295 (Accession XM_092767) is another VGAM1273 host target gene. LOC164295 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164295 BINDING SITE, designated SEQ ID:40141, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45272] Another function of VGAM1273 is therefore inhibition of LOC164295 (Accession XM_092767). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164295. LOC203429 (Accession XM_114701) is another VGAM1273 host target gene. LOC203429 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203429 BINDING SITE, designated SEQ ID:43048, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45273] Another function of VGAM1273 is therefore inhibition of LOC203429 (Accession XM_114701). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203429. LOC221272 (Accession XM_168050) is another VGAM1273 host target gene. LOC221272 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221272, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221272 BINDING SITE, designated SEQ ID:44964, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45274] Another function of VGAM1273 is therefore inhibition of

LOC221272 (Accession XM_168050). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221272. LOC91445 (Accession XM_018516) is another VGAM1273 host target gene. LOC91445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91445 BINDING SITE, designated SEQ ID:30372, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45275] Another function of VGAM1273 is therefore inhibition of LOC91445 (Accession XM_018516). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91445. LOC92497 (Accession XM_045436) is another VGAM1273 host target gene. LOC92497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC92497 BINDING SITE, designated SEQ ID:34461, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45276] Another function of VGAM1273 is therefore inhibition of LOC92497 (Accession XM_045436). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92497. LOC92689 (Accession XM_046663) is another VGAM1273 host target gene. LOC92689 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92689, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92689 BINDING SITE, designated SEQ ID:34782, to the nucleotide sequence of VGAM1273 RNA, herein designated VGAM RNA, also designated SEQ ID:3984.

[45277] Another function of VGAM1273 is therefore inhibition of LOC92689 (Accession XM_046663). Accordingly, utilities of VGAM1273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92689. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1274 (VGAM1274) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45278] VGAM1274 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1274 was detected is described hereinabove with reference to Figs. 1–8.

[45279] VGAM1274 gene, herein designated VGAM GENE, is a viral gene contained in the genome of A–2 Plaque Virus. VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45280] VGAM1274 gene encodes a VGAM1274 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1274 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1274 precursor RNA is designated SEQ ID:1260, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1260 is located at position 5481 relative to the genome of A-2 Plaque Virus.

[45281] VGAM1274 precursor RNA folds onto itself, forming VGAM1274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45282] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1274 folded precursor RNA into VGAM1274 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1274 RNA is designated SEQ ID:3985, and is provided hereinbelow with reference to the sequence listing part.

[45283] VGAM1274 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1274 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45284] VGAM1274 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1274 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1274 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1274 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[45285] The complementary binding of VGAM1274 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1274 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1274 host target RNA into VGAM1274 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45286] It is appreciated that VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1274 host target genes. The mRNA of each one of this plurality of VGAM1274 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1274 RNA, herein designated VGAM RNA, and which when bound by VGAM1274 RNA causes inhibition of translation of respective one or more

VGAM1274 host target proteins.

[45287] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1274 gene, herein designated VGAM GENE, on one or more VGAM1274 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45288] It is yet further appreciated that a function of VGAM1274 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific

functions, and accordingly utilities, of VGAM1274 correlate with, and may be deduced from, the identity of the host target genes which VGAM1274 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45289] Nucleotide sequences of the VGAM1274 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1274 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1274 are further described hereinbelow with reference to Table 1.

[45290] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1274 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1274 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45291] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1274 gene, herein designated VGAM is inhibition of expression of VGAM1274 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1274 correlate with, and may be deduced from, the identity of the target genes which VGAM1274 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45292] Inositol Polyphosphate-5-phosphatase, 75kDa (INPP5B, Accession XM_170949) is a VGAM1274 host target gene. INPP5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5B BINDING SITE, designated SEQ ID:45735, to the nucleotide sequence of VGAM1274 RNA, herein designated VGAM RNA, also designated SEQ ID:3985.

[45293] A function of VGAM1274 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 75kDa (INPP5B, Accession XM_170949), a gene which hydrolyzes the calcium-mobilizing second messenger $\text{ins}(1,4,5)\text{p3}$. Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5B. The function of INPP5B and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM50.FLJ23790 (Accession NM_144963) is another VGAM1274 host target gene. FLJ23790 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ23790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23790 BINDING SITE, designated SEQ ID:29579, to the nucleotide sequence of VGAM1274 RNA, herein designated VGAM RNA, also designated SEQ ID:3985.

[45294] Another function of VGAM1274 is therefore inhibition of FLJ23790 (Accession NM_144963). Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23790. KIAA0493 (Accession XM_034717) is another VGAM1274 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0493 BINDING SITE, designated SEQ ID:32138, to the nucleotide sequence of VGAM1274 RNA, herein designated VGAM RNA, also designated SEQ ID:3985.

[45295] Another function of VGAM1274 is therefore inhibition of KIAA0493 (Accession XM_034717). Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0596 (Accession XM_031706) is another VGAM1274 host target gene. KIAA0596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE, designated SEQ ID:31460, to the nucleotide sequence of VGAM1274 RNA, herein designated VGAM RNA, also designated SEQ ID:3985.

[45296] Another function of VGAM1274 is therefore inhibition of KIAA0596 (Accession XM_031706). Accordingly, utilities of VGAM1274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0596. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1275 (VGAM1275) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45297] VGAM1275 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1275 was detected is described hereinabove with reference to Figs. 1–8.

[45298] VGAM1275 gene, herein designated VGAM GENE, is a viral gene contained in the genome of A–2 Plaque Virus. VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45299] VGAM1275 gene encodes a VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1275 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1275 precursor RNA is designated SEQ ID:1261, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1261 is located at position 5027 relative to the

genome of A-2 Plaque Virus.

[45300] VGAM1275 precursor RNA folds onto itself, forming VGAM1275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45301] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1275 folded precursor RNA into VGAM1275 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1275 RNA is designated SEQ ID:3986, and is provided hereinbelow with reference to the sequence listing part.

[45302] VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1275 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[45303] VGAM1275 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1275 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1275 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45304] The complementary binding of VGAM1275 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1275 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1275 host target RNA into VGAM1275 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45305] It is appreciated that VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1275 host target genes. The mRNA of each one of this plurality of VGAM1275 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1275 RNA, herein designated VGAM RNA, and which when bound by VGAM1275 RNA causes inhibition of translation of respective one or more VGAM1275 host target proteins.

[45306] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1275 gene, herein designated VGAM GENE, on one or more VGAM1275 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45307] It is yet further appreciated that a function of VGAM1275 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific functions, and accordingly utilities, of VGAM1275 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1275 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45308] Nucleotide sequences of the VGAM1275 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1275 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1275 are further described hereinbelow with reference to Table 1.

[45309] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1275 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1275 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45310] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1275 gene, herein designated VGAM is inhibition of expression of VGAM1275 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1275 correlate with, and may be deduced

from, the identity of the target genes which VGAM1275 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45311] Myosin IC (MYO1C, Accession XM_028385) is a VGAM1275 host target gene. MYO1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1C BINDING SITE, designated SEQ ID:30695, to the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, also designated SEQ ID:3986.

[45312] A function of VGAM1275 is therefore inhibition of Myosin IC (MYO1C, Accession XM_028385), a gene which participates in adaptation in hair cells. Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO1C. The function of MYO1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.FLJ20209 (Accession XM_098142) is another VGAM1275 host target gene. FLJ20209 BIND-

ING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20209 BINDING SITE, designated SEQ ID:41401, to the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, also designated SEQ ID:3986.

[45313] Another function of VGAM1275 is therefore inhibition of FLJ20209 (Accession XM_098142). Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20209. FLJ21919 (Accession NM_023015) is another VGAM1275 host target gene. FLJ21919 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21919 BINDING SITE, designated SEQ ID:23277, to the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, also designated SEQ ID:3986.

[45314] Another function of VGAM1275 is therefore inhibition of

FLJ21919 (Accession NM_023015). Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21919. FLJ30678 (Accession NM_144657) is another VGAM1275 host target gene. FLJ30678 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ30678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30678 BINDING SITE, designated SEQ ID:29479, to the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, also designated SEQ ID:3986.

[45315] Another function of VGAM1275 is therefore inhibition of FLJ30678 (Accession NM_144657). Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30678. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM1275 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23706, to the nucleotide sequence of VGAM1275 RNA, herein designated VGAM RNA, also designated SEQ ID:3986.

[45316] Another function of VGAM1275 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM1275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1276 (VGAM1276) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45317] VGAM1276 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1276 was detected is described hereinabove with reference to Figs. 1–8.

[45318] VGAM1276 gene, herein designated VGAM GENE, is a viral gene contained in the genome of A-2 Plaque Virus. VGAM1276 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[45319] VGAM1276 gene encodes a VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1276 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1276 precursor RNA is designated SEQ ID:1262, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1262 is located at position 6716 relative to the genome of A-2 Plaque Virus.

[45320] VGAM1276 precursor RNA folds onto itself, forming VGAM1276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45321] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1276 folded precursor RNA into VGAM1276

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1276 RNA is designated SEQ ID:3987, and is provided hereinbelow with reference to the sequence listing part.

[45322] VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1276 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45323] VGAM1276 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1276 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1276 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45324] The complementary binding of VGAM1276 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1276 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1276 host target RNA into VGAM1276 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[45325] It is appreciated that VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1276 host target genes. The mRNA of each one of this plurality of VGAM1276 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1276 RNA, herein designated VGAM RNA, and which when bound by VGAM1276 RNA causes inhibition of translation of respective one or more VGAM1276 host target proteins.

[45326] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1276 gene, herein designated VGAM GENE, on one or more VGAM1276 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45327] It is yet further appreciated that a function of VGAM1276 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific functions, and accordingly utilities, of VGAM1276 correlate with, and may be deduced from, the identity of the host target genes which VGAM1276 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45328] Nucleotide sequences of the VGAM1276 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1276 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1276 are further described hereinbelow with reference to Table 1.

[45329] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1276 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1276 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45330] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1276 gene, herein designated VGAM is inhibition of expression of VGAM1276 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1276 correlate with, and may be deduced from, the identity of the target genes which VGAM1276 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45331] Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM_000028) is a VGAM1276 host target gene. AGL BINDING SITE1 through AGL BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGL BINDING

SITE1 through AGL BINDING SITE6, designated SEQ ID:5465, SEQ ID:6282, SEQ ID:6287, SEQ ID:6292, SEQ ID:6297 and SEQ ID:6304 respectively, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45332] A function of VGAM1276 is therefore inhibition of Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM_000028). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGL. Ankyrin 2, Neuronal (ANK2, Accession NM_020977) is another VGAM1276 host target gene. ANK2 BINDING SITE1 and ANK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK2 BINDING SITE1 and ANK2 BINDING SITE2, designated SEQ ID:21965 and SEQ ID:13134 respectively, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45333] Another function of VGAM1276 is therefore inhibition of

Ankyrin 2, Neuronal (ANK2, Accession NM_020977), a gene which attaches integral membrane proteins to cytoskeletal elements. also binds to cytoskeletal proteins. Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK2. The function of ANK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM769. Plastin 1 (I isoform) (PLS1, Accession NM_002670) is another VGAM1276 host target gene. PLS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLS1 BINDING SITE, designated SEQ ID:8540, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45334] Another function of VGAM1276 is therefore inhibition of Plastin 1 (I isoform) (PLS1, Accession NM_002670). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with PLS1. N-ethylmaleimide-sensitive Factor Attachment Protein, Gamma (NAPG, Accession XM_172983) is another VGAM1276 host target gene. NAPG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NAPG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAPG BINDING SITE, designated SEQ ID:46250, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45335] Another function of VGAM1276 is therefore inhibition of N-ethylmaleimide-sensitive Factor Attachment Protein, Gamma (NAPG, Accession XM_172983). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAPG. PRO1992 (Accession NM_014107) is another VGAM1276 host target gene. PRO1992 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO1992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1992

BINDING SITE, designated SEQ ID:15335, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45336] Another function of VGAM1276 is therefore inhibition of PRO1992 (Accession NM_014107). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1992. LOC150606 (Accession XM_097928) is another VGAM1276 host target gene. LOC150606 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150606, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150606 BINDING SITE, designated SEQ ID:41234, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45337] Another function of VGAM1276 is therefore inhibition of LOC150606 (Accession XM_097928). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150606. LOC203286 (Accession XM_117526) is another VGAM1276 host target gene. LOC203286 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203286 BINDING SITE, designated SEQ ID:43496, to the nucleotide sequence of VGAM1276 RNA, herein designated VGAM RNA, also designated SEQ ID:3987.

[45338] Another function of VGAM1276 is therefore inhibition of LOC203286 (Accession XM_117526). Accordingly, utilities of VGAM1276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1277 (VGAM1277) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45339] VGAM1277 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1277 was detected is described hereinabove with reference to Figs. 1-8.

[45340] VGAM1277 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus C. VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45341] VGAM1277 gene encodes a VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1277 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1277 precursor RNA is designated SEQ ID:1263, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1263 is located at position 156 relative to the genome of Human Enterovirus C.

[45342] VGAM1277 precursor RNA folds onto itself, forming VGAM1277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[45343] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1277 folded precursor RNA into VGAM1277 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1277 RNA is designated SEQ ID:3988, and is provided hereinbelow with reference to the sequence listing part.

[45344] VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1277 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45345] VGAM1277 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1277 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1277 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1277 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45346] The complementary binding of VGAM1277 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1277 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1277 host target RNA into VGAM1277 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45347] It is appreciated that VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1277 host target genes. The mRNA of each one of this plurality of VGAM1277 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1277 RNA, herein designated VGAM RNA, and which when bound by VGAM1277 RNA causes inhibition of translation of respective one or more VGAM1277 host target proteins.

[45348] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1277 gene, herein designated VGAM GENE, on one or more VGAM1277 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45349] It is yet further appreciated that a function of VGAM1277 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGAM1277 correlate with, and may be deduced from, the identity of the host target genes which VGAM1277 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45350] Nucleotide sequences of the VGAM1277 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1277 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1277 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1277 are further described hereinbelow with reference to Table 1.

[45351] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1277 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1277 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45352] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1277 gene, herein designated VGAM is inhibition of expression of VGAM1277 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1277 correlate with, and may be deduced from, the identity of the target genes which VGAM1277 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45353] Acid Phosphatase 1, Soluble (ACP1, Accession NM_007099) is a VGAM1277 host target gene. ACP1 BINDING SITE1 and ACP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP1 BINDING SITE1 and ACP1 BINDING SITE2, designated SEQ ID:13957 and SEQ ID:10507 respectively, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45354] A function of VGAM1277 is therefore inhibition of Acid Phosphatase 1, Soluble (ACP1, Accession NM_007099), a gene which as demonstrated in starch-gel electrophoresis. Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP1. The function of ACP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Zinc Finger Protein 179 (ZNF179, Accession NM_007148) is another VGAM1277 host target gene. ZNF179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF179 BINDING SITE, designated SEQ ID:14000, to the nucleotide

sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45355] Another function of VGAM1277 is therefore inhibition of Zinc Finger Protein 179 (ZNF179, Accession NM_007148), a gene which has zinc finger and a member of the RING finger protein family of transcription factors. Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF179. The function of ZNF179 has been established by previous studies. Kimura et al. (1997) showed, by FISH analysis of metaphase or interphase chromosomes of 6 patients with Smith–Magenis syndrome (SMS; 182290), that ZNF179 was deleted in one of the homologs, indicating possible involvement of this gene in the pathogenesis of SMS. ZNF179 was sublocalized to a site proximal to LLGL (OMIM Ref. No. 600966), which is thought to be critical to SMS

[45356] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45357] Kimura, T.; Arakawa, Y.; Inoue, S.; Fukushima, Y.; Kondo, I.; Koyama, K.; Hosoi, T.; Orimo, A.; Muramatsu, M.; Nakamura, Y.; Abe, T.; Inazawa, J. : The brain finger protein

gene (ZNF179), a member of the RING finger family, maps within the Smith–Magenis syndrome region at 17p11.2.

Am. J. Med. Genet. 69: 320–324, 1997. ; and

[45358] Matsuda, Y.; Inue, S.; Seki, N.; Hosoi, T.; Orimo, A.; Muramatsu, M.; Hori, T. : Chromosome mapping of human (ZNF179), mouse, and rat genes for brain finger protein (bfp), a member of the R.

[45359] Further studies establishing the function and utilities of ZNF179 are found in John Hopkins OMIM database record ID 601237, and in cited publications numbered 2839–2840 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14082 (Accession NM_025024) is another VGAM1277 host target gene. FLJ14082 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14082 BINDING SITE, designated SEQ ID:24610, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45360] Another function of VGAM1277 is therefore inhibition of

FLJ14082 (Accession NM_025024). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14082. KIAA1130 (Accession XM_031104) is another VGAM1277 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1130 BINDING SITE, designated SEQ ID:31281, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45361] Another function of VGAM1277 is therefore inhibition of KIAA1130 (Accession XM_031104). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1130. KIAA1536 (Accession NM_020898) is another VGAM1277 host target gene. KIAA1536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1536 BINDING SITE, designated SEQ ID:21925, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45362] Another function of VGAM1277 is therefore inhibition of KIAA1536 (Accession NM_020898). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1536. LOC121457 (Accession XM_058563) is another VGAM1277 host target gene. LOC121457 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121457 BINDING SITE, designated SEQ ID:36661, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45363] Another function of VGAM1277 is therefore inhibition of LOC121457 (Accession XM_058563). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121457. LOC146227 (Accession XM_085374) is an-

other VGAM1277 host target gene. LOC146227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146227 BINDING SITE, designated SEQ ID:38087, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45364] Another function of VGAM1277 is therefore inhibition of LOC146227 (Accession XM_085374). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146227. LOC256940 (Accession XM_172879) is another VGAM1277 host target gene. LOC256940 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256940 BINDING SITE, designated SEQ ID:46153, to the nucleotide sequence of VGAM1277 RNA, herein designated VGAM RNA, also designated SEQ ID:3988.

[45365] Another function of VGAM1277 is therefore inhibition of LOC256940 (Accession XM_172879). Accordingly, utilities of VGAM1277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256940. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1278 (VGAM1278) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45366] VGAM1278 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1278 was detected is described hereinabove with reference to Figs. 1–8.

[45367] VGAM1278 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus C. VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45368] VGAM1278 gene encodes a VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1278 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1278 precursor RNA is designated SEQ ID:1264, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1264 is located at position 1945 relative to the genome of Human Enterovirus C.

[45369] VGAM1278 precursor RNA folds onto itself, forming VGAM1278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45370] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1278 folded precursor RNA into VGAM1278 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1278 RNA is designated SEQ ID:3989, and is provided hereinbelow with reference to the sequence listing part.

[45371] VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1278 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[45372] VGAM1278 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1278 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1278 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45373] The complementary binding of VGAM1278 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1278 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1278 host target RNA into VGAM1278 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45374] It is appreciated that VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1278 host target genes. The mRNA of each one of this plurality of VGAM1278 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1278 RNA, herein designated VGAM RNA, and which when bound by VGAM1278 RNA causes inhibition of translation of respective one or more VGAM1278 host target proteins.

[45375] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1278 gene, herein designated VGAM GENE, on one or more VGAM1278 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45376] It is yet further appreciated that a function of VGAM1278 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1278 include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGAM1278 correlate with, and may be deduced from, the identity of the host target genes which VGAM1278 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45377] Nucleotide sequences of the VGAM1278 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1278 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1278 are further described hereinbelow with reference to Table 1.

[45378] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1278 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1278 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[45379] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1278 gene, herein designated VGAM is inhibition of expression of VGAM1278 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1278 correlate with, and may be deduced from, the identity of the target genes which VGAM1278 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45380] Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282) is a VGAM1278 host target gene. AP2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP2B1 BINDING SITE, designated SEQ ID:6952, to the nucleotide sequence of VGAM1278 RNA, herein designated VGAM RNA, also designated SEQ ID:3989.

[45381] A function of VGAM1278 is therefore inhibition of Adaptor-related Protein Complex 2, Beta 1 Subunit (AP2B1, Accession NM_001282), a gene which links clathrin to re-

ceptors in coated vesicles. Accordingly, utilities of VGAM1278 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP2B1. The function of AP2B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1126. Core-binding Factor, Beta Subunit (CBFB, Accession NM_001755) is another VGAM1278 host target gene. CBFB BINDING SITE1 and CBFB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBFB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFB BINDING SITE1 and CBFB BINDING SITE2, designated SEQ ID:7506 and SEQ ID:23147 respectively, to the nucleotide sequence of VGAM1278 RNA, herein designated VGAM RNA, also designated SEQ ID:3989.

[45382] Another function of VGAM1278 is therefore inhibition of Core-binding Factor, Beta Subunit (CBFB, Accession NM_001755), a gene which is beta subunit of the transcription factor CBF which causes leukemia. Accordingly, utilities of VGAM1278 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CBFB. The function of CBFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98.MBLL39 (Accession NM_144778) is another VGAM1278 host target gene. MBLL39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBLL39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBLL39 BINDING SITE, designated SEQ ID:29573, to the nucleotide sequence of VGAM1278 RNA, herein designated VGAM RNA, also designated SEQ ID:3989.

[45383] Another function of VGAM1278 is therefore inhibition of MBLL39 (Accession NM_144778). Accordingly, utilities of VGAM1278 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBLL39. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1279 (VGAM1279) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[45384] VGAM1279 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1279 was detected is described hereinabove with reference to Figs. 1–8.

[45385] VGAM1279 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus C. VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45386] VGAM1279 gene encodes a VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1279 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1279 precursor RNA is designated SEQ ID:1265, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1265 is located at position 1075 relative to the genome of Human Enterovirus C.

[45387] VGAM1279 precursor RNA folds onto itself, forming VGAM1279 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45388] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1279 folded precursor RNA into VGAM1279 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1279 RNA is designated SEQ ID:3990, and is provided hereinbelow with reference to the sequence listing part.

[45389] VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1279 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45390] VGAM1279 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1279 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1279 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45391] The complementary binding of VGAM1279 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1279 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1279 host target RNA into VGAM1279 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45392] It is appreciated that VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1279 host target genes. The mRNA of each one of this plurality of VGAM1279 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1279 RNA, herein designated VGAM RNA, and which when bound by VGAM1279 RNA causes inhibition of translation of respective one or more VGAM1279 host target proteins.

[45393] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1279 gene, herein designated VGAM GENE, on one or more VGAM1279 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45394] It is yet further appreciated that a function of VGAM1279 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGAM1279 correlate with, and may be deduced from, the identity of the host target genes which VGAM1279 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[45395] Nucleotide sequences of the VGAM1279 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1279 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1279 are further described hereinbelow with reference to Table 1.

[45396] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1279 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1279 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45397] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1279 gene, herein designated VGAM is inhibition of expression of VGAM1279 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1279 correlate with, and may be deduced from, the identity of the target genes which VGAM1279 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45398] Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575) is a VGAM1279 host target gene. C17orf31 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:18996, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45399] A function of VGAM1279 is therefore inhibition of Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf31. FLJ12960 (Accession NM_024638) is another VGAM1279 host target gene. FLJ12960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE, designated

SEQ ID:23913, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45400] Another function of VGAM1279 is therefore inhibition of FLJ12960 (Accession NM_024638). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12960. G Protein Pathway Suppressor 2 (GPS2, Accession NM_004489) is another VGAM1279 host target gene. GPS2 BINDING SITE1 and GPS2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GPS2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPS2 BINDING SITE1 and GPS2 BINDING SITE2, designated SEQ ID:10824 and SEQ ID:42146 respectively, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45401] Another function of VGAM1279 is therefore inhibition of G Protein Pathway Suppressor 2 (GPS2, Accession NM_004489). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with GPS2. LOC126430 (Accession XM_065082) is another VGAM1279 host target gene. LOC126430 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC126430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126430 BINDING SITE, designated SEQ ID:37276, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45402] Another function of VGAM1279 is therefore inhibition of LOC126430 (Accession XM_065082). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126430. LOC144501 (Accession XM_096612) is another VGAM1279 host target gene. LOC144501 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144501 BINDING SITE, designated SEQ ID:40428, to

the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45403] Another function of VGAM1279 is therefore inhibition of LOC144501 (Accession XM_096612). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144501. LOC148398 (Accession XM_086174) is another VGAM1279 host target gene. LOC148398 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148398 BINDING SITE, designated SEQ ID:38530, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45404] Another function of VGAM1279 is therefore inhibition of LOC148398 (Accession XM_086174). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148398. LOC167153 (Accession XM_094312) is another VGAM1279 host target gene. LOC167153 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC167153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC167153 BINDING SITE, designated SEQ ID:40230, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45405] Another function of VGAM1279 is therefore inhibition of LOC167153 (Accession XM_094312). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC167153. LOC199221 (Accession XM_087310) is another VGAM1279 host target gene. LOC199221 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199221 BINDING SITE, designated SEQ ID:39163, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45406] Another function of VGAM1279 is therefore inhibition of LOC199221 (Accession XM_087310). Accordingly, utilities

of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199221. LOC201911 (Accession XM_117339) is another VGAM1279 host target gene. LOC201911 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201911, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201911 BINDING SITE, designated SEQ ID:43389, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45407] Another function of VGAM1279 is therefore inhibition of LOC201911 (Accession XM_117339). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201911. LOC220565 (Accession XM_165417) is another VGAM1279 host target gene. LOC220565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220565 BINDING SITE, designated SEQ ID:43632, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45408] Another function of VGAM1279 is therefore inhibition of LOC220565 (Accession XM_165417). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220565. LOC254228 (Accession XM_171123) is another VGAM1279 host target gene. LOC254228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254228 BINDING SITE, designated SEQ ID:45917, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45409] Another function of VGAM1279 is therefore inhibition of LOC254228 (Accession XM_171123). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254228. LOC256310 (Accession XM_172813) is another VGAM1279 host target gene. LOC256310 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256310 BINDING SITE, designated SEQ ID:46094, to the nucleotide sequence of VGAM1279 RNA, herein designated VGAM RNA, also designated SEQ ID:3990.

[45410] Another function of VGAM1279 is therefore inhibition of LOC256310 (Accession XM_172813). Accordingly, utilities of VGAM1279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256310. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1280 (VGAM1280) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45411] VGAM1280 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1280 was detected is described hereinabove with reference to Figs. 1-8.

[45412] VGAM1280 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus C. VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45413] VGAM1280 gene encodes a VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1280 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1280 precursor RNA is designated SEQ ID:1266, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1266 is located at position 1669 relative to the genome of Human Enterovirus C.

[45414] VGAM1280 precursor RNA folds onto itself, forming VGAM1280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[45415] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1280 folded precursor RNA into VGAM1280 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1280 RNA is designated SEQ ID:3991, and is provided hereinbelow with reference to the sequence listing part.

[45416] VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1280 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45417] VGAM1280 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1280 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1280 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1280 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45418] The complementary binding of VGAM1280 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1280 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1280 host target RNA into VGAM1280 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45419] It is appreciated that VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1280 host target genes. The mRNA of each one of this plurality of VGAM1280 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1280 RNA, herein designated VGAM RNA, and which when bound by VGAM1280 RNA causes inhibition of translation of respective one or more VGAM1280 host target proteins.

[45420] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1280 gene, herein designated VGAM GENE, on one or more VGAM1280 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45421] It is yet further appreciated that a function of VGAM1280 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGAM1280 correlate with, and may be deduced from, the identity of the host target genes which VGAM1280 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45422] Nucleotide sequences of the VGAM1280 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1280 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1280 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1280 are further described hereinbelow with reference to Table 1.

[45423] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1280 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1280 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45424] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1280 gene, herein designated VGAM is inhibition of expression of VGAM1280 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1280 correlate with, and may be deduced from, the identity of the target genes which VGAM1280 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45425] Activin A Receptor, Type I (ACVR1, Accession NM_001105) is a VGAM1280 host target gene. ACVR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ACVR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ACVR1 BINDING SITE, designated SEQ ID:6763, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45426] A function of VGAM1280 is therefore inhibition of Activin A Receptor, Type I (ACVR1, Accession NM_001105), a gene which Activin receptor-like kinase; similar to activin, TGF-beta, and C. elegans daf-1 receptors. Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACVR1. The function of ACVR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217.AF3P21 (Accession NM_016453) is another VGAM1280 host target gene. AF3P21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AF3P21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AF3P21 BINDING SITE, designated SEQ ID:18568, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ

ID:3991.

[45427] Another function of VGAM1280 is therefore inhibition of AF3P21 (Accession NM_016453), a gene which has an important role in stress fiber formation induced by active diaphanous protein homolog 1 (drf1). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AF3P21. The function of AF3P21 has been established by previous studies. Sano et al. (2000) identified the AF3p21 gene as a novel fusion partner of the MLL gene (OMIM Ref. No. 159555) in a 23-year-old patient who developed therapy-related leukemia (AML, FAB M5b) with t(3;11)(p21;q23). Hayakawa et al. (2001) further characterized the AF3p21 gene. AF3p21 encodes a nuclear protein consisting of 722 amino acids with an SH3 domain, a proline-rich domain, and a bipartite nuclear localization signal. The protein's SH3 domain has high homology with that of FYN (OMIM Ref. No. 137025). Hayakawa et al. (2001) found that in DNA from the patient's leukemic cells, intron 6 of the MLL gene was fused at a point upstream of exon 1 in the AF3p21 gene, and that the der(11) chromosome formed an MLL-AF3p21 fusion transcript in leukemic cells, whereas the der(3) chromosome did not

form any fusion transcript. Dot blot RNA analysis showed that the AF3p21 gene was expressed in all adult and embryonic human tissues examined, including bone marrow, brain, liver, thymus, lung, and skeletal muscle. Northern blot analysis of HeLa cell RNA detected a 3.5-kb transcript. The protein has an apparent molecular weight of 80 kD and is localized exclusively in the cell nucleus. These results suggested that AF3p21 protein plays a role in signal transduction in the nucleus. Hayakawa et al. (2001) determined that the AF3p21 gene on 3p21 is 19 kb long and consists of 13 exons.

[45428] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45429] Hayakawa, A.; Matsuda, Y.; Daibata, M.; Nakamura, H.; Sano, K. : Genomic organization, tissue expression, and cellular localization of AF3p21, a fusion partner of MLL in therapy-related leukemia. *Genes Chromosomes Cancer* 30: 364–374, 2001. ; and

[45430] Sano, K.; Hayakawa, A.; Piao, J.-H.; Kosaka, Y.; Nakamura, H. : Novel SH3 protein encoded by the AF3p21 gene is fused to the mixed lineage leukemia protein in a therapy-related leukemia.

[45431] Further studies establishing the function and utilities of AF3P21 are found in John Hopkins OMIM database record ID 606671, and in cited publications numbered 6457–6458 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Frizzled Homolog 6 (Drosophila) (FZD6, Accession NM_003506) is another VGAM1280 host target gene. FZD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD6 BINDING SITE, designated SEQ ID:9596, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45432] Another function of VGAM1280 is therefore inhibition of Frizzled Homolog 6 (Drosophila) (FZD6, Accession NM_003506). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD6. Growth Arrest-specific 11 (GAS11, Accession NM_001481) is another VGAM1280 host target gene. GAS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by GAS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS11 BINDING SITE, designated SEQ ID:7223, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45433] Another function of VGAM1280 is therefore inhibition of Growth Arrest-specific 11 (GAS11, Accession NM_001481). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS11. Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834) is another VGAM1280 host target gene. GRIN2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2B BINDING SITE, designated SEQ ID:6490, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45434] Another function of VGAM1280 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN2B. BH-protocadherin (brain-heart) (PCDH7, Accession NM_002589) is another VGAM1280 host target gene. PCDH7 BINDING SITE1 through PCDH7 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH7 BINDING SITE1 through PCDH7 BINDING SITE3, designated SEQ ID:8451, SEQ ID:26215 and SEQ ID:26219 respectively, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45435] Another function of VGAM1280 is therefore inhibition of BH-protocadherin (brain-heart) (PCDH7, Accession NM_002589). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH7. Ret Proto-oncogene (multiple endocrine neoplasia and medullary

thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM_020975) is another VGAM1280 host target gene. RET BINDING SITE1 and RET BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RET, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RET BINDING SITE1 and RET BINDING SITE2, designated SEQ ID:21961 and SEQ ID:17508 respectively, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45436] Another function of VGAM1280 is therefore inhibition of Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease) (RET, Accession NM_020975), a gene which transduces signals for cell growth and differentiation. Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RET. The function of RET and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.SH3-domain Binding Protein 4 (SH3BP4,

Accession NM_014521) is another VGAM1280 host target gene. SH3BP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP4 BINDING SITE, designated SEQ ID:15855, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45437] Another function of VGAM1280 is therefore inhibition of SH3-domain Binding Protein 4 (SH3BP4, Accession NM_014521), a gene which is of unknown function, contains SH3-domain binding protein 4; similar to the EH-binding protein. Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP4. The function of SH3BP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Chromosome 1 Open Reading Frame 8 (C1orf8, Accession NM_004872) is another VGAM1280 host target gene. C1orf8 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by C1orf8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf8 BINDING SITE, designated SEQ ID:11299, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45438] Another function of VGAM1280 is therefore inhibition of Chromosome 1 Open Reading Frame 8 (C1orf8, Accession NM_004872). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf8. Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM_020248) is another VGAM1280 host target gene. CTNNBIP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CTNNBIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNNBIP1 BINDING SITE, designated SEQ ID:21546, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45439] Another function of VGAM1280 is therefore inhibition of Catenin, Beta Interacting Protein 1 (CTNNBIP1, Accession NM_020248). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNNBIP1. DKFZP434E2135 (Accession NM_030804) is another VGAM1280 host target gene. DKFZP434E2135 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434E2135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434E2135 BINDING SITE, designated SEQ ID:25117, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45440] Another function of VGAM1280 is therefore inhibition of DKFZP434E2135 (Accession NM_030804). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2135. DKFZp761N0624 (Accession NM_032295) is another VGAM1280 host target gene. DKFZp761N0624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DKFZp761N0624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N0624 BINDING SITE, designated SEQ ID:26072, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45441] Another function of VGAM1280 is therefore inhibition of DKFZp761N0624 (Accession NM_032295). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761N0624. DKFZp762E1312 (Accession NM_018410) is another VGAM1280 host target gene. DKFZp762E1312 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp762E1312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762E1312 BINDING SITE, designated SEQ ID:20452, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45442] Another function of VGAM1280 is therefore inhibition of

DKFZp762E1312 (Accession NM_018410). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762E1312. F-box Only Protein 24 (FBXO24, Accession NM_012172) is another VGAM1280 host target gene. FBXO24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO24 BINDING SITE, designated SEQ ID:14465, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45443] Another function of VGAM1280 is therefore inhibition of F-box Only Protein 24 (FBXO24, Accession NM_012172). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO24. FLJ20651 (Accession NM_017919) is another VGAM1280 host target gene. FLJ20651 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20651, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20651 BINDING SITE, designated SEQ ID:19576, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45444] Another function of VGAM1280 is therefore inhibition of FLJ20651 (Accession NM_017919). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20651. FLJ21168 (Accession NM_025073) is another VGAM1280 host target gene. FLJ21168 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21168 BINDING SITE, designated SEQ ID:24672, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45445] Another function of VGAM1280 is therefore inhibition of FLJ21168 (Accession NM_025073). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ21168. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM1280 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:28923 and SEQ ID:17402 respectively, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45446] Another function of VGAM1280 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA1550 (Accession XM_039393) is another VGAM1280 host target gene. KIAA1550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1550, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1550 BINDING SITE, designated SEQ ID:33074, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45447] Another function of VGAM1280 is therefore inhibition of KIAA1550 (Accession XM_039393). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1550. KIAA1729 (Accession XM_114418) is another VGAM1280 host target gene. KIAA1729 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1729 BINDING SITE, designated SEQ ID:42951, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45448] Another function of VGAM1280 is therefore inhibition of KIAA1729 (Accession XM_114418). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1729. MGC4663 (Accession NM_024514) is another VGAM1280 host target gene. MGC4663 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC4663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4663 BINDING SITE, designated SEQ ID:23717, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45449] Another function of VGAM1280 is therefore inhibition of MGC4663 (Accession NM_024514). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4663. RIS1 (Accession XM_087461) is another VGAM1280 host target gene. RIS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RIS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIS1 BINDING SITE, designated SEQ ID:39273, to the nucleotide sequence of

VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45450] Another function of VGAM1280 is therefore inhibition of RIS1 (Accession XM_087461). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIS1. Zinc Finger Protein 220 (ZNF220, Accession NM_006766) is another VGAM1280 host target gene. ZNF220 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF220 BINDING SITE, designated SEQ ID:13632, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45451] Another function of VGAM1280 is therefore inhibition of Zinc Finger Protein 220 (ZNF220, Accession NM_006766). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF220. LOC116064 (Accession XM_057296) is another VGAM1280 host target gene. LOC116064 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LOC116064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116064 BINDING SITE, designated SEQ ID:36497, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45452] Another function of VGAM1280 is therefore inhibition of LOC116064 (Accession XM_057296). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116064. LOC158293 (Accession XM_088541) is another VGAM1280 host target gene. LOC158293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158293 BINDING SITE, designated SEQ ID:39805, to the nucleotide sequence of VGAM1280 RNA, herein designated VGAM RNA, also designated SEQ ID:3991.

[45453] Another function of VGAM1280 is therefore inhibition of

LOC158293 (Accession XM_088541). Accordingly, utilities of VGAM1280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158293. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1281 (VGAM1281) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45454] VGAM1281 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1281 was detected is described hereinabove with reference to Figs. 1-8.

[45455] VGAM1281 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Virus Q. VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45456] VGAM1281 gene encodes a VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1281 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1281 precursor RNA is designated SEQ ID:1267, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1267 is located at position 1984 relative to the genome of Beet Virus Q.

- [45457] VGAM1281 precursor RNA folds onto itself, forming VGAM1281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45458] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1281 folded precursor RNA into VGAM1281 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1281 RNA is designated SEQ ID:3992, and

is provided hereinbelow with reference to the sequence listing part.

[45459] VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1281 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[45460] VGAM1281 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1281 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1281 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45461] The complementary binding of VGAM1281 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1281 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1281 host target RNA into VGAM1281 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45462] It is appreciated that VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1281 host target genes. The mRNA of each one of this plurality of VGAM1281 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1281 RNA, herein designated VGAM RNA, and which when bound by VGAM1281 RNA causes inhibition of translation of respective one or more VGAM1281 host target proteins.

[45463] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1281 gene, herein designated VGAM GENE, on one or more VGAM1281 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45464] It is yet further appreciated that a function of VGAM1281 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities, of VGAM1281 correlate with, and may be deduced from, the identity of the host target genes which VGAM1281 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45465] Nucleotide sequences of the VGAM1281 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1281 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1281 are further described hereinbelow with reference to Table 1.

[45466] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1281 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1281 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45467] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1281 gene, herein designated VGAM is inhibition of expression of VGAM1281 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1281 correlate with, and may be deduced from, the identity of the target genes which VGAM1281 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45468] LFG (Accession XM_084780) is a VGAM1281 host target gene. LFG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFG BINDING SITE, designated SEQ ID:37698, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45469] A function of VGAM1281 is therefore inhibition of LFG (Accession XM_084780). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LFG. Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804) is another VGAM1281 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in

the 5` untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:44843, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45470] Another function of VGAM1281 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449) is another VGAM1281 host target gene. RFX5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6049, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45471] Another function of VGAM1281 is therefore inhibition of

Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449), a gene which activates transcription from class II MHC promoters. Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Sorting Nexin 6 (SNX6, Accession NM_021249) is another VGAM1281 host target gene. SNX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX6 BINDING SITE, designated SEQ ID:22218, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45472] Another function of VGAM1281 is therefore inhibition of Sorting Nexin 6 (SNX6, Accession NM_021249). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX6. TAR (HIV) RNA Binding Protein 2 (TARBP2,

Accession NM_134324) is another VGAM1281 host target gene. TARBP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TARBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TARBP2 BINDING SITE, designated SEQ ID:28630, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45473] Another function of VGAM1281 is therefore inhibition of TAR (HIV) RNA Binding Protein 2 (TARBP2, Accession NM_134324), a gene which is involved in the regulation of HIV replication. Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TARBP2. The function of TARBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Thiopurine S-methyltransferase (TPMT, Accession NM_000367) is another VGAM1281 host target gene. TPMT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TPMT,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPMT BINDING SITE, designated SEQ ID:5937, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45474] Another function of VGAM1281 is therefore inhibition of Thiopurine S-methyltransferase (TPMT, Accession NM_000367), a gene which catalyzes the s-methylation of thiopurine drugs such as 6-mercaptopurine. Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPMT. The function of TPMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM682. Amino adipate-semialdehyde Dehydrogenase-phosphopantetheinyl Transferase (AASDHPPT, Accession NM_015423) is another VGAM1281 host target gene. AASDHPPT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AASDHPPT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of AASDHPPT BINDING SITE, designated SEQ ID:17723, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45475] Another function of VGAM1281 is therefore inhibition of Amino adipate-semialdehyde Dehydrogenase-phosphopantetheinyl Transferase (AASDHPPT, Accession NM_015423). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AASDHPPT. UDP-Gal:betaGal Beta 1,3-galactosyltransferase Polypeptide 6 (B3GALT6, Accession NM_080605) is another VGAM1281 host target gene. B3GALT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B3GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT6 BINDING SITE, designated SEQ ID:27923, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45476] Another function of VGAM1281 is therefore inhibition of UDP-Gal:betaGal Beta 1,3-galactosyltransferase Polypep-

tide 6 (B3GALT6, Accession NM_080605). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT6. Death-associated Protein Kinase 2 (DA PK2, Accession NM_014326) is another VGAM1281 host target gene. DAPK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DAPK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAPK2 BINDING SITE, designated SEQ ID:15632, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45477] Another function of VGAM1281 is therefore inhibition of Death-associated Protein Kinase 2 (DA PK2, Accession NM_014326). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAPK2. DKFZP761F241 (Accession NM_031455) is another VGAM1281 host target gene. DKFZP761F241 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP761F241, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761F241 BINDING SITE, designated SEQ ID:25475, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45478] Another function of VGAM1281 is therefore inhibition of DKFZP761F241 (Accession NM_031455). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761F241. Enabled Homolog (Drosophila) (ENAH, Accession NM_018212) is another VGAM1281 host target gene. ENAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAH BINDING SITE, designated SEQ ID:20122, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45479] Another function of VGAM1281 is therefore inhibition of Enabled Homolog (Drosophila) (ENAH, Accession

NM_018212). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAH. FLJ30574 (Accession NM_144629) is another VGAM1281 host target gene.

FLJ30574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30574 BINDING SITE, designated SEQ ID:29446, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45480] Another function of VGAM1281 is therefore inhibition of FLJ30574 (Accession NM_144629). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30574. Oxysterol Binding Protein-like 10 (OSBPL10, Accession NM_017784) is another VGAM1281 host target gene. OSBPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL10 BINDING SITE, designated SEQ ID:19416, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45481] Another function of VGAM1281 is therefore inhibition of Oxysterol Binding Protein-like 10 (OSBPL10, Accession NM_017784). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL10. ZF (Accession NM_021212) is another VGAM1281 host target gene. ZF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZF BINDING SITE, designated SEQ ID:22190, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45482] Another function of VGAM1281 is therefore inhibition of ZF (Accession NM_021212). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZF.

LOC116068 (Accession XM_057302) is another VGAM1281 host target gene. LOC116068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116068 BINDING SITE, designated SEQ ID:36501, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45483] Another function of VGAM1281 is therefore inhibition of LOC116068 (Accession XM_057302). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116068. LOC151121 (Accession XM_087102) is another VGAM1281 host target gene. LOC151121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151121 BINDING SITE, designated SEQ ID:39052, to the nucleotide sequence of VGAM1281 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3992.

[45484] Another function of VGAM1281 is therefore inhibition of LOC151121 (Accession XM_087102). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151121. LOC201411 (Accession XM_031946) is another VGAM1281 host target gene. LOC201411 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201411 BINDING SITE, designated SEQ ID:31526, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45485] Another function of VGAM1281 is therefore inhibition of LOC201411 (Accession XM_031946). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201411. LOC254085 (Accession XM_171189) is another VGAM1281 host target gene. LOC254085 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254085, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254085 BINDING SITE, designated SEQ ID:45972, to the nucleotide sequence of VGAM1281 RNA, herein designated VGAM RNA, also designated SEQ ID:3992.

[45486] Another function of VGAM1281 is therefore inhibition of LOC254085 (Accession XM_171189). Accordingly, utilities of VGAM1281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254085. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1282 (VGAM1282) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45487] VGAM1282 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1282 was detected is described hereinabove with reference to Figs. 1-8.

[45488] VGAM1282 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Virus Q. VGAM1282

host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45489] VGAM1282 gene encodes a VGAM1282 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1282 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1282 precursor RNA is designated SEQ ID:1268, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1268 is located at position 3568 relative to the genome of Beet Virus Q.

[45490] VGAM1282 precursor RNA folds onto itself, forming VGAM1282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45491] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1282 folded precursor RNA into VGAM1282

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1282 RNA is designated SEQ ID:3993, and is provided hereinbelow with reference to the sequence listing part.

[45492] VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1282 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45493] VGAM1282 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1282 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1282 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45494] The complementary binding of VGAM1282 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1282 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1282 host target RNA into VGAM1282 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[45495] It is appreciated that VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1282 host target genes. The mRNA of each one of this plurality of VGAM1282 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1282 RNA, herein designated VGAM RNA, and which when bound by VGAM1282 RNA causes inhibition of translation of respective one or more VGAM1282 host target proteins.

[45496] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1282 gene, herein designated VGAM GENE, on one or more VGAM1282 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45497] It is yet further appreciated that a function of VGAM1282 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities, of VGAM1282 correlate with, and may be deduced from, the identity of the host target genes which VGAM1282 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45498] Nucleotide sequences of the VGAM1282 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1282 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1282 are further described hereinbelow with reference to Table 1.

[45499] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1282 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1282 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45500] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1282 gene, herein designated VGAM is inhibition of expression of VGAM1282 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1282 correlate with, and may be deduced from, the identity of the target genes which VGAM1282 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45501] FLJ10726 (Accession NM_018195) is a VGAM1282 host target gene. FLJ10726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10726 BINDING SITE, designated SEQ ID:20058, to the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3993.

[45502] A function of VGAM1282 is therefore inhibition of FLJ10726 (Accession NM_018195). Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10726. FLJ23153 (Accession NM_024636) is another VGAM1282 host target gene. FLJ23153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23153 BINDING SITE, designated SEQ ID:23908, to the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, also designated SEQ ID:3993.

[45503] Another function of VGAM1282 is therefore inhibition of FLJ23153 (Accession NM_024636). Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23153. KIAA1036 (Accession NM_014909) is another VGAM1282 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17127, to the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, also designated SEQ ID:3993.

[45504] Another function of VGAM1282 is therefore inhibition of KIAA1036 (Accession NM_014909). Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. KIAA1577 (Accession XM_035299) is another VGAM1282 host target gene. KIAA1577 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1577 BINDING SITE, designated SEQ ID:32212, to the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, also designated SEQ ID:3993.

[45505] Another function of VGAM1282 is therefore inhibition of KIAA1577 (Accession XM_035299). Accordingly, utilities of VGAM1282 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1577. LOC91308 (Accession XM_037600) is another VGAM1282 host target gene. LOC91308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91308 BINDING SITE, designated SEQ ID:32657, to the nucleotide sequence of VGAM1282 RNA, herein designated VGAM RNA, also designated SEQ ID:3993.

[45506] Another function of VGAM1282 is therefore inhibition of LOC91308 (Accession XM_037600). Accordingly, utilities of VGAM1282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91308. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1283 (VGAM1283) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45507] VGAM1283 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1283 was detected is described hereinabove with reference to Figs. 1–8.

[45508] VGAM1283 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Virus Q. VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45509] VGAM1283 gene encodes a VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1283 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1283 precursor RNA is designated SEQ ID:1269, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1269 is located at position 3671 relative to the genome of Beet Virus Q.

[45510] VGAM1283 precursor RNA folds onto itself, forming VGAM1283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45511] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1283 folded precursor RNA into VGAM1283 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1283 RNA is designated SEQ ID:3994, and is provided hereinbelow with reference to the sequence listing part.

[45512] VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1283 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45513] VGAM1283 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1283 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1283 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45514] The complementary binding of VGAM1283 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1283 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1283 host target RNA into VGAM1283 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45515] It is appreciated that VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1283 host target genes. The mRNA of each one of this plurality of VGAM1283 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1283 RNA, herein designated VGAM RNA, and which when bound by VGAM1283 RNA causes inhibition of translation of respective one or more VGAM1283 host target proteins.

[45516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1283 gene, herein designated VGAM GENE, on one or more VGAM1283 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45517] It is yet further appreciated that a function of VGAM1283 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities, of VGAM1283 correlate with, and may be deduced from, the identity of the host target genes which VGAM1283 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45518] Nucleotide sequences of the VGAM1283 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1283 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1283 are further described hereinbelow with reference to Table 1.

[45519] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1283 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1283 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45520] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1283 gene, herein designated VGAM is inhibition of expression of VGAM1283 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1283 correlate with, and may be deduced from, the identity of the target genes which VGAM1283 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45521] S-adenosylhomocysteine Hydrolase (AHCY, Accession NM_000687) is a VGAM1283 host target gene. AHCY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AHCY, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AHCY BINDING SITE, designated SEQ ID:6344, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45522] A function of VGAM1283 is therefore inhibition of S-adenosylhomocysteine Hydrolase (AHCY, Accession NM_000687). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AHCY. Archain 1 (ARCN1, Accession NM_001655) is another VGAM1283 host target gene. ARCN1 BINDING SITE1 and ARCN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ARCN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARCN1 BINDING SITE1 and ARCN1 BINDING SITE2, designated SEQ ID:7367 and SEQ ID:7369 respectively, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45523] Another function of VGAM1283 is therefore inhibition of

Archain 1 (ARCN1, Accession NM_001655), a gene which plays a fundamental role in eukaryotic cell biology. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARCN1. The function of ARCN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1226. Cell Division Cycle 42 (GTP binding protein, 25kDa) (CDC42, Accession NM_001791) is another VGAM1283 host target gene. CDC42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42 BINDING SITE, designated SEQ ID:7542, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45524] Another function of VGAM1283 is therefore inhibition of Cell Division Cycle 42 (GTP binding protein, 25kDa) (CDC42, Accession NM_001791). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CDC42. Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1, Accession NM_004360) is another VGAM1283 host target gene. CDH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH1 BINDING SITE, designated SEQ ID:10566, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45525] Another function of VGAM1283 is therefore inhibition of Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1, Accession NM_004360). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH1. Cyclin-dependent Kinase 5, Regulatory Subunit 2 (p39) (CDK5R2, Accession NM_003936) is another VGAM1283 host target gene. CDK5R2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK5R2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CDK5R2 BINDING SITE, designated SEQ ID:10043, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45526] Another function of VGAM1283 is therefore inhibition of Cyclin-dependent Kinase 5, Regulatory Subunit 2 (p39) (CDK5R2, Accession NM_003936), a gene which acts as a regulatory subunit for the cyclin-dependent CDK5. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK5R2. The function of CDK5R2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM403. Dedicator of Cyto-kinesis 1 (DOCK1, Accession NM_001380) is another VGAM1283 host target gene. DOCK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOCK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOCK1 BINDING SITE, designated SEQ ID:7052, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA,

also designated SEQ ID:3994.

[45527] Another function of VGAM1283 is therefore inhibition of Dedicator of Cyto-kinesis 1 (DOCK1, Accession NM_001380), a gene which may function in the extension of cell surfaces. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOCK1. The function of DOCK1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM564. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_138619) is another VGAM1283 host target gene. GGA3 BINDING SITE1 and GGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA3 BINDING SITE1 and GGA3 BINDING SITE2, designated SEQ ID:28902 and SEQ ID:15199 respectively, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45528] Another function of VGAM1283 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_138619), a gene which may play a role in the regulation of membrane traffic through the trans-golgi network. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA3. The function of GGA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM353. Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962) is another VGAM1283 host target gene. IL22RA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL22RA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL22RA2 BINDING SITE, designated SEQ ID:27524, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45529] Another function of VGAM1283 is therefore inhibition of Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession

NM_052962), a gene which induces the production of acute-phase reactants. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL22RA2. The function of IL22RA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167. Potassium Voltage-gated Channel, Shal-related Subfamily, Member 2 (KCND2, Accession NM_012281) is another VGAM1283 host target gene. KCND2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND2 BINDING SITE, designated SEQ ID:14612, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45530] Another function of VGAM1283 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 2 (KCND2, Accession NM_012281), a gene which is prominent in the repolarization phase of the action potential. Accordingly, utilities of VGAM1283 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with KCND2. The function of KCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM449.Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450) is another VGAM1283 host target gene.

KLHL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL3 BINDING SITE, designated SEQ ID:42268, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45531] Another function of VGAM1283 is therefore inhibition of Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL3. LIM Domain Only 1 (rhombotin 1) (LMO1, Accession NM_002315) is another VGAM1283 host target gene. LMO1 BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by LMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO1 BINDING SITE, designated SEQ ID:8128, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45532] Another function of VGAM1283 is therefore inhibition of LIM Domain Only 1 (rhombotin 1) (LMO1, Accession NM_002315). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO1. Lysyl Oxidase-like 2 (LOXL2, Accession NM_002318) is another VGAM1283 host target gene. LOXL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOXL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL2 BINDING SITE, designated SEQ ID:8132, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45533] Another function of VGAM1283 is therefore inhibition of Lysyl Oxidase-like 2 (LOXL2, Accession NM_002318), a gene which may have roles in senescence and cell adhesion. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOXL2. The function of LOXL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM147. Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269) is another VGAM1283 host target gene. NR2E1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NR2E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR2E1 BINDING SITE, designated SEQ ID:9280, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45534] Another function of VGAM1283 is therefore inhibition of Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269), a gene which may be required for brain development and be involved in the regulation of

retinal development . Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR2E1. The function of NR2E1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM689. Phosphodiesterase 4A, CAMP-specific (phosphodiesterase E2 duncce homolog, Drosophila) (PDE4A, Accession NM_006202) is another VGAM1283 host target gene. PDE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4A BINDING SITE, designated SEQ ID:12877, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45535] Another function of VGAM1283 is therefore inhibition of Phosphodiesterase 4A, CAMP-specific (phosphodiesterase E2 duncce homolog, Drosophila) (PDE4A, Accession NM_006202), a gene which is a CAMP-specific phosphodiesterase . Accordingly, utilities of VGAM1283 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4A. The function of PDE4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1214. Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession NM_002608) is another VGAM1283 host target gene. PDGFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFB BINDING SITE, designated SEQ ID:8471, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45536] Another function of VGAM1283 is therefore inhibition of Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession NM_002608), a gene which plays an important role in stimulating adjacent cells to grow and thereby heal the wound. Accordingly, utilities of VGAM1283 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with PDGFB. The function of PDGFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Protein Phosphatase 2, Regulatory Subunit B (B56), Delta Isoform (PPP2R5D, Accession NM_006245) is another VGAM1283 host target gene. PPP2R5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5D BINDING SITE, designated SEQ ID:12916, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45537] Another function of VGAM1283 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Delta Isoform (PPP2R5D, Accession NM_006245), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5D. The function of PPP2R5D and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM96. Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Alpha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944) is another VGAM1283 host target gene. PPP3CA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP3CA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP3CA BINDING SITE, designated SEQ ID:6647, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45538] Another function of VGAM1283 is therefore inhibition of Protein Phosphatase 3 (formerly 2B), Catalytic Subunit, Alpha Isoform (calcineurin A alpha) (PPP3CA, Accession NM_000944), a gene which is the catalytic subunit of calcium-dependent, calmodulin-stimulated protein phosphatase. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP3CA. The function of PPP3CA and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM497. Periaxin (PRX, Accession NM_020956) is another VGAM1283 host target gene. PRX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRX BINDING SITE, designated SEQ ID:21939, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45539] Another function of VGAM1283 is therefore inhibition of Periaxin (PRX, Accession NM_020956), a gene which seems to be required for maintenance of peripheral nerve myelin sheath. may have a role in axon-glial interactions, possibly by interacting with the cytoplasmic domains of integral membrane proteins such as myelin-associated glycoprotein in the periaxonal regions of the schwann cell plasma membrane. may have a role in the early phases of myelin deposition. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRX. The function of

PRX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM476. Phosphatase and Tensin Homolog (mutated in multiple advanced cancers 1) (PTEN, Accession NM_000314) is another VGAM1283 host target gene. PTEN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTEN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTEN BINDING SITE, designated SEQ ID:5852, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45540] Another function of VGAM1283 is therefore inhibition of Phosphatase and Tensin Homolog (mutated in multiple advanced cancers 1) (PTEN, Accession NM_000314). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTEN. Paxillin (PXN, Accession NM_002859) is another VGAM1283 host target gene. PXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXN, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXN BINDING SITE, designated SEQ ID:8758, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45541] Another function of VGAM1283 is therefore inhibition of Paxillin (PXN, Accession NM_002859), a gene which may be involved in p53-dependent apoptosis. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXN. The function of PXN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132. Retinal G Protein Coupled Receptor (RGR, Accession NM_002921) is another VGAM1283 host target gene. RGR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGR BINDING SITE, designated SEQ ID:8826, to the nucleotide sequence of VGAM1283 RNA, herein

designated VGAM RNA, also designated SEQ ID:3994.

[45542] Another function of VGAM1283 is therefore inhibition of Retinal G Protein Coupled Receptor (RGR, Accession NM_002921), a gene which catalyse the isomerization of the chromophore by a retinochrome-like mechanism and act as a receptor for all-trans-and 11-cis-retinal. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGR. The function of RGR has been established by previous studies. Jiang et al. (1993) identified an opsin-related gene that is preferentially expressed at high levels in the RPE and Muller cells of the neural retina. The gene encodes a putative RPE-retinal G protein-coupled receptor (RGR) with 7 transmembrane segments. The putative receptor most closely resembled the subfamily of visual pigments and retinochromes. Shen et al. (1994) found that the amino acid sequence of RGR in humans is 86% identical to that of bovine RGR and that a lysine residue, analogous to the retinaldehyde attachment site of rhodopsin (OMIM Ref. No. 180380), is conserved in the seventh transmembrane domain of RGR in both species. The human gene spans 14.8 kb and is split into 7 exons. The structure of the gene is distinct from that of the visual

pigment genes. Shen et al. (1994) suggested that the RGR gene represents the earliest independent branch of the vertebrate opsin gene family. A second form of human RGR in retina was predicted by alternative splicing of its precursor mRNA. This RGR variant resulted from the alternative use of an internal acceptor splice site in the second intron of the human gene, and it contained an insertion of 4 amino acids in the connecting loop between the second and third transmembrane domains. Morimura et al. (1999) reported 2 mutations in RGR in patients with photoreceptor degeneration, indicating that RGR is essential to the retina. Using a single-strand conformation technique, Morimura et al. (1999) searched for mutations in the exons and flanking intron sequences of RGR in 182 unrelated patients with dominantly inherited retinitis pigmentosa, 182 with recessive retinitis pigmentosa, 383 with simplex retinitis pigmentosa (sporadic cases), 45 with Leber congenital amaurosis, 28 with retinitis punctata albescens, 22 with choroidal sclerosis, and 93–95 normal controls. One index patient with recessive RP was homozygous for a ser66-to-arg missense mutation (600342.0001). A second patient, originally diagnosed with choroidal sclerosis, was heterozygous for a 1-bp in-

sertion in codon gly275 (GGA-to-GGGA) near the 3-prime end of the coding region (600342.0002). Both affected sibs were heterozygotes and an unaffected sib was homozygous wildtype. The deceased father was said to have been affected, making it likely that the retinal degeneration in this family is dominantly inherited. Morimura et al. (1999) detected no alteration of the other allele in the 2 affected individuals or in unaffected members of this family.

[45543] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45544] Mutations in RGR, encoding a light-sensitive opsin homologue, in patients with retinitis pigmentosa. (Letter) Nature Genet. 23: 393-394, 1999. ; and

[45545] Shen, D.; Jiang, M.; Hao, W.; Tao, L.; Salazar, M.; Fong, H. K. W. : A human opsin-related gene that encodes a retinaldehyde-binding protein. Biochemistry 33: 13117-13125, 1994.

[45546] Further studies establishing the function and utilities of RGR are found in John Hopkins OMIM database record ID 600342, and in cited publications numbered 8287-8291 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. Solute Carrier Family 2 (facilitated glucose transporter), Member 1 (SLC2A1, Accession NM_006516) is another VGAM1283 host target gene. SLC2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A1 BINDING SITE, designated SEQ ID:13265, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45547] Another function of VGAM1283 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 1 (SLC2A1, Accession NM_006516). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A1. Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459) is another VGAM1283 host target gene. SLC30A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC30A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC30A3 BINDING SITE, designated SEQ ID:9528, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45548] Another function of VGAM1283 is therefore inhibition of Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC30A3. Uncoupling Protein 2 (mitochondrial, proton carrier) (UCP2, Accession NM_003355) is another VGAM1283 host target gene. UCP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by UCP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UCP2 BINDING SITE, designated SEQ ID:9381, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45549] Another function of VGAM1283 is therefore inhibition of Uncoupling Protein 2 (mitochondrial, proton carrier)

(UCP2, Accession NM_003355), a gene which is an inner mitochondrial membrane transporter and uncouples electron transport from oxidative phosphorylation. Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UCP2. The function of UCP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1135. Zinc Finger Protein 175 (ZNF175, Accession NM_007147) is another VGAM1283 host target gene. ZNF175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF175 BINDING SITE, designated SEQ ID:13999, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45550] Another function of VGAM1283 is therefore inhibition of Zinc Finger Protein 175 (ZNF175, Accession NM_007147). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with ZNF175. A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM_016248) is another VGAM1283 host target gene. AKAP11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP11 BINDING SITE, designated SEQ ID:18368, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45551] Another function of VGAM1283 is therefore inhibition of A Kinase (PRKA) Anchor Protein 11 (AKAP11, Accession NM_016248). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP11. ARP5 (Accession XM_049490) is another VGAM1283 host target gene. ARP5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARP5 BINDING SITE, designated SEQ ID:35440, to the nu-

cleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45552] Another function of VGAM1283 is therefore inhibition of ARP5 (Accession XM_049490). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARP5. BCAA (Accession NM_016374) is another VGAM1283 host target gene. BCAA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BCAA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCAA BINDING SITE, designated SEQ ID:18512, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45553] Another function of VGAM1283 is therefore inhibition of BCAA (Accession NM_016374). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCAA. Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575) is another VGAM1283 host target gene. C17orf31 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:19009, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45554] Another function of VGAM1283 is therefore inhibition of Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf31. Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837) is another VGAM1283 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16859, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ

ID:3994.

[45555] Another function of VGAM1283 is therefore inhibition of Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966) is another VGAM1283 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27537, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45556] Another function of VGAM1283 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. Chromosome 9 Open Reading Frame 5 (C9orf5, Accession NM_032012)

is another VGAM1283 host target gene. C9orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C9orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf5 BINDING SITE, designated SEQ ID:25718, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45557] Another function of VGAM1283 is therefore inhibition of Chromosome 9 Open Reading Frame 5 (C9orf5, Accession NM_032012). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf5. C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 9 (CLECSF9, Accession NM_014358) is another VGAM1283 host target gene. CLECSF9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLECSF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF9 BINDING SITE, designated SEQ ID:15690, to the

nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45558] Another function of VGAM1283 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 9 (CLECSF9, Accession NM_014358). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF9. Cyclin M1 (CNNM1, Accession NM_020348) is another VGAM1283 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21611, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45559] Another function of VGAM1283 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM_020348). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. DKFZP564C103 (Accession NM_015654) is

another VGAM1283 host target gene. DKFZP564C103 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564C103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564C103 BINDING SITE, designated SEQ ID:17902, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45560] Another function of VGAM1283 is therefore inhibition of DKFZP564C103 (Accession NM_015654). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C103. DKFZP586I2223 (Accession NM_015438) is another VGAM1283 host target gene. DKFZP586I2223 BINDING SITE1 through DKFZP586I2223 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP586I2223, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586I2223 BINDING SITE1

through DKFZP586I2223 BINDING SITE3, designated SEQ ID:17734, SEQ ID:28018 and SEQ ID:28020 respectively, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45561] Another function of VGAM1283 is therefore inhibition of DKFZP586I2223 (Accession NM_015438). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586I2223. Fidgetin (FIGN, Accession XM_171005) is another VGAM1283 host target gene. FIGN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FIGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FIGN BINDING SITE, designated SEQ ID:45776, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45562] Another function of VGAM1283 is therefore inhibition of Fidgetin (FIGN, Accession XM_171005). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FIGN. FLJ10139 (Accession NM_018005) is another

VGAM1283 host target gene. FLJ10139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10139 BINDING SITE, designated SEQ ID:19735, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45563] Another function of VGAM1283 is therefore inhibition of FLJ10139 (Accession NM_018005). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10139. FLJ12704 (Accession NM_024998) is another VGAM1283 host target gene. FLJ12704 BINDING SITE1 and FLJ12704 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12704, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12704 BINDING SITE1 and FLJ12704 BINDING SITE2, designated SEQ ID:24564 and SEQ ID:24566 respectively, to the nucleotide sequence of

VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45564] Another function of VGAM1283 is therefore inhibition of FLJ12704 (Accession NM_024998). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12704. FLJ14213 (Accession NM_024841) is another VGAM1283 host target gene. FLJ14213 BINDING SITE1 and FLJ14213 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ14213, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14213 BINDING SITE1 and FLJ14213 BINDING SITE2, designated SEQ ID:24252 and SEQ ID:24253 respectively, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45565] Another function of VGAM1283 is therefore inhibition of FLJ14213 (Accession NM_024841). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14213. FLJ14768 (Accession NM_032836) is another

VGAM1283 host target gene. FLJ14768 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14768 BINDING SITE, designated SEQ ID:26615, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45566] Another function of VGAM1283 is therefore inhibition of FLJ14768 (Accession NM_032836). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14768. FLJ20281 (Accession XM_165663) is another VGAM1283 host target gene. FLJ20281 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20281 BINDING SITE, designated SEQ ID:43725, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45567] Another function of VGAM1283 is therefore inhibition of FLJ20281 (Accession XM_165663). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20281. FLJ20802 (Accession NM_017959) is another VGAM1283 host target gene. FLJ20802 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20802 BINDING SITE, designated SEQ ID:19675, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45568] Another function of VGAM1283 is therefore inhibition of FLJ20802 (Accession NM_017959). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20802. FLJ22215 (Accession XM_173021) is another VGAM1283 host target gene. FLJ22215 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22215 BINDING SITE, designated SEQ ID:46283, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45569] Another function of VGAM1283 is therefore inhibition of FLJ22215 (Accession XM_173021). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22215. Glucocorticoid Induced Transcript 1 (GLCCI1, Accession XM_166529) is another VGAM1283 host target gene. GLCCI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GLCCI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLCCI1 BINDING SITE, designated SEQ ID:44480, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45570] Another function of VGAM1283 is therefore inhibition of Glucocorticoid Induced Transcript 1 (GLCCI1, Accession XM_166529). Accordingly, utilities of VGAM1283 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with GLCCI1. Glycoprotein A33 (transmembrane) (GPA33, Accession NM_005814) is another VGAM1283 host target gene. GPA33 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPA33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPA33 BINDING SITE, designated SEQ ID:12407, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45571] Another function of VGAM1283 is therefore inhibition of Glycoprotein A33 (transmembrane) (GPA33, Accession NM_005814). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPA33. Hippocalcin Like 4 (HPCAL4, Accession NM_016257) is another VGAM1283 host target gene. HPCAL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPCAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of HPCAL4 BINDING SITE, designated SEQ ID:18388, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45572] Another function of VGAM1283 is therefore inhibition of Hippocalcin Like 4 (HPCAL4, Accession NM_016257). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL4. KIAA0268 (Accession XM_046126) is another VGAM1283 host target gene. KIAA0268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0268 BINDING SITE, designated SEQ ID:34685, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45573] Another function of VGAM1283 is therefore inhibition of KIAA0268 (Accession XM_046126). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0268. KIAA0523 (Accession XM_041964) is another VGAM1283 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33639, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45574] Another function of VGAM1283 is therefore inhibition of KIAA0523 (Accession XM_041964). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. KIAA0939 (Accession XM_030524) is another VGAM1283 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31058, to the nucleotide sequence of VGAM1283 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3994.

[45575] Another function of VGAM1283 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA0953 (Accession XM_039733) is another VGAM1283 host target gene. KIAA0953 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0953, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0953 BINDING SITE, designated SEQ ID:33172, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45576] Another function of VGAM1283 is therefore inhibition of KIAA0953 (Accession XM_039733). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0953. KIAA1280 (Accession XM_045766) is another VGAM1283 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34556, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45577] Another function of VGAM1283 is therefore inhibition of KIAA1280 (Accession XM_045766). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1301 (Accession XM_038999) is another VGAM1283 host target gene. KIAA1301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1301 BINDING SITE, designated SEQ ID:32980, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45578] Another function of VGAM1283 is therefore inhibition of KIAA1301 (Accession XM_038999). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1301. KIAA1363 (Accession XM_045056) is another VGAM1283 host target gene. KIAA1363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1363 BINDING SITE, designated SEQ ID:34336, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45579] Another function of VGAM1283 is therefore inhibition of KIAA1363 (Accession XM_045056). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1363. KIAA1655 (Accession XM_039442) is another VGAM1283 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33093, to the

nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45580] Another function of VGAM1283 is therefore inhibition of KIAA1655 (Accession XM_039442). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1655. KIAA1879 (Accession XM_056635) is another VGAM1283 host target gene. KIAA1879 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1879 BINDING SITE, designated SEQ ID:36417, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45581] Another function of VGAM1283 is therefore inhibition of KIAA1879 (Accession XM_056635). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1879. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1283 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12791, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45582] Another function of VGAM1283 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. MGC10960 (Accession NM_032653) is another VGAM1283 host target gene. MGC10960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10960 BINDING SITE, designated SEQ ID:26381, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45583] Another function of VGAM1283 is therefore inhibition of MGC10960 (Accession NM_032653). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10960. MGC12760 (Accession NM_032723) is another VGAM1283 host target gene. MGC12760 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12760 BINDING SITE, designated SEQ ID:26449, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45584] Another function of VGAM1283 is therefore inhibition of MGC12760 (Accession NM_032723). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12760. MGC5139 (Accession XM_058587) is another VGAM1283 host target gene. MGC5139 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5139, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5139 BINDING SITE, designated SEQ ID:36675, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45585] Another function of VGAM1283 is therefore inhibition of MGC5139 (Accession XM_058587). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5139. NIBAN (Accession NM_022083) is another VGAM1283 host target gene. NIBAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIBAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIBAN BINDING SITE, designated SEQ ID:22632, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45586] Another function of VGAM1283 is therefore inhibition of NIBAN (Accession NM_022083). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIBAN.

NSG-X (Accession NM_014411) is another VGAM1283 host target gene. NSG-X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NSG-X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NSG-X BINDING SITE, designated SEQ ID:15755, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45587] Another function of VGAM1283 is therefore inhibition of NSG-X (Accession NM_014411). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NSG-X. Nucleoredoxin (NXN, Accession NM_022463) is another VGAM1283 host target gene. NXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXN BINDING SITE, designated SEQ ID:22806, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3994.

[45588] Another function of VGAM1283 is therefore inhibition of Nucleoredoxin (NXN, Accession NM_022463). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXN. poly(rC) Binding Protein 3 (PCBP3, Accession NM_020528) is another VGAM1283 host target gene. PCBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCBP3 BINDING SITE, designated SEQ ID:21752, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45589] Another function of VGAM1283 is therefore inhibition of poly(rC) Binding Protein 3 (PCBP3, Accession NM_020528). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCBP3. PI4KII (Accession NM_018425) is another VGAM1283 host target gene. PI4KII BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by PI4KII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PI4KII BINDING SITE, designated SEQ ID:20484, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45590] Another function of VGAM1283 is therefore inhibition of PI4KII (Accession NM_018425). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PI4KII. PRO0659 (Accession NM_014138) is another VGAM1283 host target gene. PRO0659 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0659, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0659 BINDING SITE, designated SEQ ID:15405, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45591] Another function of VGAM1283 is therefore inhibition of PRO0659 (Accession NM_014138). Accordingly, utilities of

VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0659. Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM_130842) is another VGAM1283 host target gene. PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRN2 BINDING SITE1 and PTPRN2 BINDING SITE2, designated SEQ ID:28367 and SEQ ID:28372 respectively, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45592] Another function of VGAM1283 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, N Polypeptide 2 (PTPRN2, Accession NM_130842). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRN2. Sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase) (SIAT9, Accession NM_003896) is another

VGAM1283 host target gene. SIAT9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIAT9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIAT9 BINDING SITE, designated SEQ ID:9979, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45593] Another function of VGAM1283 is therefore inhibition of Sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase) (SIAT9, Accession NM_003896). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIAT9. Tigger Transposable Element Derived 1 (TIGD1, Accession XM_114293) is another VGAM1283 host target gene. TIGD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TIGD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIGD1 BINDING SITE, designated SEQ ID:42847, to the nucleotide se-

quence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45594] Another function of VGAM1283 is therefore inhibition of Tigger Transposable Element Derived 1 (TIGD1, Accession XM_114293). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIGD1. WD Repeat Domain 9 (WDR9, Accession NM_033656) is another VGAM1283 host target gene. WDR9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WDR9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR9 BINDING SITE, designated SEQ ID:27390, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45595] Another function of VGAM1283 is therefore inhibition of WD Repeat Domain 9 (WDR9, Accession NM_033656). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR9. LOC112616 (Accession NM_138410) is another VGAM1283 host target gene.

LOC112616 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112616, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112616 BINDING SITE, designated SEQ ID:28775, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45596] Another function of VGAM1283 is therefore inhibition of LOC112616 (Accession NM_138410). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112616. LOC126364 (Accession XM_065047) is another VGAM1283 host target gene. LOC126364 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126364 BINDING SITE, designated SEQ ID:37274, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45597] Another function of VGAM1283 is therefore inhibition of LOC126364 (Accession XM_065047). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126364. LOC145739 (Accession XM_085222) is another VGAM1283 host target gene. LOC145739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145739 BINDING SITE, designated SEQ ID:37964, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45598] Another function of VGAM1283 is therefore inhibition of LOC145739 (Accession XM_085222). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145739. LOC145845 (Accession XM_096884) is another VGAM1283 host target gene. LOC145845 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145845, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145845 BINDING SITE, designated SEQ ID:40619, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45599] Another function of VGAM1283 is therefore inhibition of LOC145845 (Accession XM_096884). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145845. LOC146909 (Accession XM_085634) is another VGAM1283 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38270, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45600] Another function of VGAM1283 is therefore inhibition of LOC146909 (Accession XM_085634). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146909. LOC146957 (Accession XM_085652) is another VGAM1283 host target gene. LOC146957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146957 BINDING SITE, designated SEQ ID:38282, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45601] Another function of VGAM1283 is therefore inhibition of LOC146957 (Accession XM_085652). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146957. LOC147791 (Accession XM_097293) is another VGAM1283 host target gene. LOC147791 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147791, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147791 BINDING SITE, designated SEQ ID:40859, to the nucleotide sequence of VGAM1283 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3994.

[45602] Another function of VGAM1283 is therefore inhibition of LOC147791 (Accession XM_097293). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147791. LOC148710 (Accession XM_097506) is another VGAM1283 host target gene. LOC148710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148710 BINDING SITE, designated SEQ ID:40895, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45603] Another function of VGAM1283 is therefore inhibition of LOC148710 (Accession XM_097506). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148710. LOC149372 (Accession XM_086509) is another VGAM1283 host target gene. LOC149372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149372, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38727, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45604] Another function of VGAM1283 is therefore inhibition of LOC149372 (Accession XM_086509). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC150319 (Accession XM_086816) is another VGAM1283 host target gene. LOC150319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150319 BINDING SITE, designated SEQ ID:38898, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45605] Another function of VGAM1283 is therefore inhibition of LOC150319 (Accession XM_086816). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150319. LOC151154 (Accession XM_098008) is another VGAM1283 host target gene. LOC151154 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151154 BINDING SITE, designated SEQ ID:41304, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45606] Another function of VGAM1283 is therefore inhibition of LOC151154 (Accession XM_098008). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151154. LOC152245 (Accession XM_098182) is another VGAM1283 host target gene. LOC152245 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152245 BINDING SITE, designated SEQ ID:41450, to

the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45607] Another function of VGAM1283 is therefore inhibition of LOC152245 (Accession XM_098182). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152245. LOC152271 (Accession XM_087419) is another VGAM1283 host target gene. LOC152271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152271 BINDING SITE, designated SEQ ID:39241, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45608] Another function of VGAM1283 is therefore inhibition of LOC152271 (Accession XM_087419). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152271. LOC154860 (Accession XM_098623) is another VGAM1283 host target gene. LOC154860 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC154860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154860 BINDING SITE, designated SEQ ID:41734, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45609] Another function of VGAM1283 is therefore inhibition of LOC154860 (Accession XM_098623). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154860. LOC157681 (Accession XM_088363) is another VGAM1283 host target gene. LOC157681 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157681 BINDING SITE, designated SEQ ID:39643, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45610] Another function of VGAM1283 is therefore inhibition of LOC157681 (Accession XM_088363). Accordingly, utilities

of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157681. LOC164714 (Accession XM_104657) is another VGAM1283 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42177, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45611] Another function of VGAM1283 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC196337 (Accession XM_113696) is another VGAM1283 host target gene. LOC196337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC196337 BINDING SITE, designated SEQ ID:42362, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45612] Another function of VGAM1283 is therefore inhibition of LOC196337 (Accession XM_113696). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196337. LOC200982 (Accession XM_117305) is another VGAM1283 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43373, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45613] Another function of VGAM1283 is therefore inhibition of LOC200982 (Accession XM_117305). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. LOC203350 (Accession XM_117536) is another VGAM1283 host target gene. LOC203350 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43539, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45614] Another function of VGAM1283 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC222128 (Accession XM_166560) is another VGAM1283 host target gene. LOC222128 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222128 BINDING SITE, designated SEQ ID:44539, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45615] Another function of VGAM1283 is therefore inhibition of

LOC222128 (Accession XM_166560). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222128. LOC254085 (Accession XM_171189) is another VGAM1283 host target gene. LOC254085 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254085 BINDING SITE, designated SEQ ID:45973, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45616] Another function of VGAM1283 is therefore inhibition of LOC254085 (Accession XM_171189). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254085. LOC51107 (Accession NM_016022) is another VGAM1283 host target gene. LOC51107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC51107 BINDING SITE, designated SEQ ID:18096, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45617] Another function of VGAM1283 is therefore inhibition of LOC51107 (Accession NM_016022). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51107. LOC51308 (Accession NM_016606) is another VGAM1283 host target gene. LOC51308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51308 BINDING SITE, designated SEQ ID:18711, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45618] Another function of VGAM1283 is therefore inhibition of LOC51308 (Accession NM_016606). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51308. LOC63928 (Accession NM_022097) is another

VGAM1283 host target gene. LOC63928 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC63928, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC63928 BINDING SITE, designated SEQ ID:22636, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45619] Another function of VGAM1283 is therefore inhibition of LOC63928 (Accession NM_022097). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC63928. LOC85414 (Accession NM_033102) is another VGAM1283 host target gene. LOC85414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC85414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85414 BINDING SITE, designated SEQ ID:26950, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45620] Another function of VGAM1283 is therefore inhibition of LOC85414 (Accession NM_033102). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85414. LOC90678 (Accession NM_138361) is another VGAM1283 host target gene. LOC90678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90678 BINDING SITE, designated SEQ ID:28749, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45621] Another function of VGAM1283 is therefore inhibition of LOC90678 (Accession NM_138361). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90678. LOC91151 (Accession NM_033208) is another VGAM1283 host target gene. LOC91151 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91151, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91151 BINDING SITE, designated SEQ ID:27055, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45622] Another function of VGAM1283 is therefore inhibition of LOC91151 (Accession NM_033208). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91151. LOC91301 (Accession XM_037564) is another VGAM1283 host target gene. LOC91301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91301 BINDING SITE, designated SEQ ID:32653, to the nucleotide sequence of VGAM1283 RNA, herein designated VGAM RNA, also designated SEQ ID:3994.

[45623] Another function of VGAM1283 is therefore inhibition of LOC91301 (Accession XM_037564). Accordingly, utilities of VGAM1283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1284 (VGAM1284) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45624] VGAM1284 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1284 was detected is described hereinabove with reference to Figs. 1–8.

[45625] VGAM1284 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus A. VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45626] VGAM1284 gene encodes a VGAM1284 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1284 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1284 precursor RNA is designated SEQ ID:1270, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1270 is located at position 4771 relative to the genome of Human Enterovirus A.

- [45627] VGAM1284 precursor RNA folds onto itself, forming VGAM1284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [45628] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1284 folded precursor RNA into VGAM1284 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1284 RNA is designated SEQ ID:3995, and is provided hereinbelow with reference to the sequence listing part.

[45629] VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1284 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45630] VGAM1284 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1284 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1284 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45631] The complementary binding of VGAM1284 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1284 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1284 host target RNA into VGAM1284 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45632] It is appreciated that VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1284 host target genes. The mRNA of each one of this plurality of VGAM1284 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1284 RNA, herein designated VGAM RNA, and which when bound by VGAM1284 RNA causes

inhibition of translation of respective one or more VGAM1284 host target proteins.

[45633] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1284 gene, herein designated VGAM GENE, on one or more VGAM1284 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45634] It is yet further appreciated that a function of VGAM1284 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1284 include diagnosis, prevention and

treatment of viral infection by Human Enterovirus A. Specific functions, and accordingly utilities, of VGAM1284 correlate with, and may be deduced from, the identity of the host target genes which VGAM1284 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45635] Nucleotide sequences of the VGAM1284 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1284 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1284 are further described hereinbelow with reference to Table 1.

[45636] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1284 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1284 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45637] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1284 gene, herein designated VGAM is inhibition of expression of VGAM1284 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1284 correlate with, and may be deduced from, the identity of the target genes which VGAM1284 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45638] Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM_006380) is a VGAM1284 host target gene. APPBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APPBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APPBP2 BINDING SITE, designated SEQ ID:13080, to the nucleotide sequence of VGAM1284 RNA, herein designated VGAM RNA, also designated SEQ ID:3995.

[45639] A function of VGAM1284 is therefore inhibition of Amyloid Beta Precursor Protein (cytoplasmic tail) Binding Protein 2 (APPBP2, Accession NM_006380), a gene which interacts with the basolateral sorting signal of amyloid precursor protein. Accordingly, utilities of VGAM1284 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APPBP2. The function of

APPBP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM525. POU Domain, Class 2, Associating Factor 1 (POU2AF1, Accession NM_006235) is another VGAM1284 host target gene. POU2AF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU2AF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU2AF1 BINDING SITE, designated SEQ ID:12890, to the nucleotide sequence of VGAM1284 RNA, herein designated VGAM RNA, also designated SEQ ID:3995.

[45640] Another function of VGAM1284 is therefore inhibition of POU Domain, Class 2, Associating Factor 1 (POU2AF1, Accession NM_006235), a gene which is a transcriptional coactivator that specifically associates with either oct1 or oct2. Accordingly, utilities of VGAM1284 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU2AF1. The function of POU2AF1 and its association with various diseases and clinical conditions, has been established by previous stud-

ies, as described hereinabove with reference to VGAM171.LOC149401 (Accession XM_086511) is another VGAM1284 host target gene. LOC149401 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149401 BINDING SITE, designated SEQ ID:38739, to the nucleotide sequence of VGAM1284 RNA, herein designated VGAM RNA, also designated SEQ ID:3995.

[45641] Another function of VGAM1284 is therefore inhibition of LOC149401 (Accession XM_086511). Accordingly, utilities of VGAM1284 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149401. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1285 (VGAM1285) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45642] VGAM1285 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1285 was detected is described hereinabove with reference to Figs. 1-8.

[45643] VGAM1285 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Virus Q. VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45644] VGAM1285 gene encodes a VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1285 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1285 precursor RNA is designated SEQ ID:1271, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1271 is located at position 460 relative to the genome of Beet Virus Q.

[45645] VGAM1285 precursor RNA folds onto itself, forming VGAM1285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45646] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1285 folded precursor RNA into VGAM1285 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1285 RNA is designated SEQ ID:3996, and is provided hereinbelow with reference to the sequence listing part.

[45647] VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1285 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45648] VGAM1285 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1285 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1285 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45649] The complementary binding of VGAM1285 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1285 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1285 host target RNA into VGAM1285 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45650] It is appreciated that VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1285 host target genes. The mRNA of each one of this plurality of VGAM1285 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1285 RNA, herein designated VGAM RNA, and which when bound by VGAM1285 RNA causes inhibition of translation of respective one or more VGAM1285 host target proteins.

[45651] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1285 gene, herein designated VGAM GENE, on one or more VGAM1285 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45652] It is yet further appreciated that a function of VGAM1285 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities, of VGAM1285 correlate with, and may be deduced from, the identity of the host target genes which VGAM1285 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45653] Nucleotide sequences of the VGAM1285 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1285 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1285 are further described hereinbelow with reference to Table 1.

[45654] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1285 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1285 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45655] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1285 gene, herein designated VGAM is inhibition of expression of VGAM1285 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1285 correlate with, and may be deduced from, the identity of the target genes which VGAM1285 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45656] Alpha-1-B Glycoprotein (A1BG, Accession NM_130786) is a VGAM1285 host target gene. A1BG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by A1BG, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A1BG BINDING SITE, designated SEQ ID:28276, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45657] A function of VGAM1285 is therefore inhibition of Alpha-1-B Glycoprotein (A1BG, Accession NM_130786), a gene which a plasma protein of unknown function. Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A1BG. The function of A1BG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is another VGAM1285 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ

ID:12883, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45658] Another function of VGAM1285 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117. Chromobox Homolog 6 (CBX6, Accession NM_014292) is another VGAM1285 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15577, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45659] Another function of VGAM1285 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM_014292). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. Centaurin, Gamma 2 (CENTG2, Accession NM_014914) is another VGAM1285 host target gene. CENTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG2 BINDING SITE, designated SEQ ID:17157, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45660] Another function of VGAM1285 is therefore inhibition of Centaurin, Gamma 2 (CENTG2, Accession NM_014914). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG2. DKFZP434A0131 (Accession NM_018991) is another VGAM1285 host target gene. DKFZP434A0131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by DKFZP434A0131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434A0131 BINDING SITE, designated SEQ ID:21062, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45661] Another function of VGAM1285 is therefore inhibition of DKFZP434A0131 (Accession NM_018991). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434A0131. Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379) is another VGAM1285 host target gene. KCNV1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNV1 BINDING SITE, designated SEQ ID:15711, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45662] Another function of VGAM1285 is therefore inhibition of

Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNV1. MARKL1 (Accession NM_031417) is another VGAM1285 host target gene. MARKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MARKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MARKL1 BINDING SITE, designated SEQ ID:25396, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45663] Another function of VGAM1285 is therefore inhibition of MARKL1 (Accession NM_031417). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MARKL1. LOC148293 (Accession XM_086138) is another VGAM1285 host target gene. LOC148293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148293, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148293 BINDING SITE, designated SEQ ID:38518, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45664] Another function of VGAM1285 is therefore inhibition of LOC148293 (Accession XM_086138). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148293. LOC220018 (Accession XM_167816) is another VGAM1285 host target gene. LOC220018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220018 BINDING SITE, designated SEQ ID:44857, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45665] Another function of VGAM1285 is therefore inhibition of LOC220018 (Accession XM_167816). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220018. LOC86651 (Accession XM_044052) is another VGAM1285 host target gene. LOC86651 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC86651, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC86651 BINDING SITE, designated SEQ ID:34099, to the nucleotide sequence of VGAM1285 RNA, herein designated VGAM RNA, also designated SEQ ID:3996.

[45666] Another function of VGAM1285 is therefore inhibition of LOC86651 (Accession XM_044052). Accordingly, utilities of VGAM1285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC86651. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1286 (VGAM1286) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45667] VGAM1286 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1286 was detected is described hereinabove with reference to Figs. 1–8.

[45668] VGAM1286 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Enterovirus A. VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45669] VGAM1286 gene encodes a VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1286 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1286 precursor RNA is designated SEQ ID:1272, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1272 is located at position 1767 relative to the genome of Human Enterovirus A.

[45670] VGAM1286 precursor RNA folds onto itself, forming VGAM1286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45671] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1286 folded precursor RNA into VGAM1286 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1286 RNA is designated SEQ ID:3997, and is provided hereinbelow with reference to the sequence listing part.

[45672] VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1286 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45673] VGAM1286 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1286 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1286 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45674] The complementary binding of VGAM1286 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1286 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1286 host target RNA into VGAM1286 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45675] It is appreciated that VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1286 host target genes. The mRNA of each one of this plurality of VGAM1286 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1286 RNA, herein designated VGAM RNA, and which when bound by VGAM1286 RNA causes inhibition of translation of respective one or more VGAM1286 host target proteins.

[45676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1286 gene, herein designated VGAM GENE, on one or more VGAM1286 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45677] It is yet further appreciated that a function of VGAM1286 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of viral infection by Human Enterovirus A. Specific functions, and accordingly utilities, of VGAM1286 correlate with, and may be deduced from, the identity of the host target genes which VGAM1286 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45678] Nucleotide sequences of the VGAM1286 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1286 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1286 are further described hereinbelow with reference to Table 1.

[45679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1286 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1286 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45680] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1286 gene, herein designated VGAM is inhibition of expression of VGAM1286 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1286 correlate with, and may be deduced from, the identity of the target genes which VGAM1286 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45681] Chromosome 1 Open Reading Frame 6 (C1orf6, Accession NM_020131) is a VGAM1286 host target gene. C1orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf6, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf6 BINDING SITE, designated SEQ ID:21328, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45682] A function of VGAM1286 is therefore inhibition of Chromosome 1 Open Reading Frame 6 (C1orf6, Accession NM_020131), a gene which may link ataxin-1 with the chaperone and ubiquitin/proteasome pathways . Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf6. The function of C1orf6 has been established by previous studies. By a yeast 2-hybrid screen of an adult human brain cDNA library, Davidson et al. (2000) isolated cDNA clones which they used to assemble a complete cDNA encoding the 601-amino acid ataxin-1 ubiquitin-like interacting protein (A1U). Sequence comparison revealed that A1U contains an N-terminal ubiquitin-like region, placing it within a large family of similar proteins. In addition, A1U shows substantial homology to human UBQLN2 (OMIM Ref. No. 300264), a protein that binds the ATPase domain of the HSP70-like STCH protein (OMIM

Ref. No. 601100). Expression analyses demonstrated that A1U mRNA is widely expressed as a 4.0-kb transcript and is present in Purkinje cells, the primary site of spinocerebellar ataxia-1 (SCA1; 164400) cerebellar pathology. The A1U protein localized to the nucleus and cytoplasm of transfected COS-1 cells. Sequences important for the transport of A1U into the nucleus appeared to lie within the C terminus. In the nucleus, A1U colocalized with mutant ataxin-1 (ATX1; 601556), further demonstrating that A1U interacts with ataxin-1. Davidson et al. (2000) suggested that A1U may link ataxin-1 with the chaperone and ubiquitin/proteasome pathways and that ataxin-1 may function in the formation and regulation of multimeric protein complexes within the nucleus.

[45683] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45684] Davidson, J. D.; Riley, B.; Burright, E.N.; Duvick, L.A.; Zoghbi, H.Y.; Orr, H. T. : Identification and characterization of an ataxin-1-interacting protein: A1Up, a ubiquitin-like nuclear protein. Hum. Molec. Genet. 9: 2305-2312, 2000. ; and

[45685] Fogli, A.; Giglio, S.; Arrigo, G.; Lo Nigro, C.; Zollo, M.; Vig-

giano, L.; Rocchi, M.; Archidiacono, N.; Zuffardi, O.; Carozzo, R. : Identification of two paralogous regions mapping to.

[45686] Further studies establishing the function and utilities of C1orf6 are found in John Hopkins OMIM database record ID 605440, and in cited publications numbered 4794 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Peroxisomal Biogenesis Factor 3 (PEX3, Accession NM_003630) is another VGAM1286 host target gene. PEX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX3 BINDING SITE, designated SEQ ID:9690, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45687] Another function of VGAM1286 is therefore inhibition of Peroxisomal Biogenesis Factor 3 (PEX3, Accession NM_003630). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX3. BCMP1 (Accession

NM_031442) is another VGAM1286 host target gene.

BCMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCMP1 BINDING SITE, designated SEQ ID:25454, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45688] Another function of VGAM1286 is therefore inhibition of BCMP1 (Accession NM_031442). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCMP1. DKFZP434F1735 (Accession NM_015590) is another VGAM1286 host target gene. DKFZP434F1735 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434F1735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F1735 BINDING SITE, designated SEQ ID:17857, to the nucleotide sequence of VGAM1286

RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45689] Another function of VGAM1286 is therefore inhibition of DKFZP434F1735 (Accession NM_015590). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F1735. FLJ21106 (Accession NM_025097) is another VGAM1286 host target gene. FLJ21106 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21106 BINDING SITE, designated SEQ ID:24733, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45690] Another function of VGAM1286 is therefore inhibition of FLJ21106 (Accession NM_025097). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21106. KIAA0914 (Accession NM_014883) is another VGAM1286 host target gene. KIAA0914 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0914 BINDING SITE, designated SEQ ID:17032, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45691] Another function of VGAM1286 is therefore inhibition of KIAA0914 (Accession NM_014883). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0914. KIAA1287 (Accession XM_085753) is another VGAM1286 host target gene. KIAA1287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1287 BINDING SITE, designated SEQ ID:38324, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45692] Another function of VGAM1286 is therefore inhibition of KIAA1287 (Accession XM_085753). Accordingly, utilities

of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1287. Mitochondrial Ribosomal Protein S14 (MRPS14, Accession NM_022100) is another VGAM1286 host target gene. MRPS14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS14 BINDING SITE, designated SEQ ID:22641, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45693] Another function of VGAM1286 is therefore inhibition of Mitochondrial Ribosomal Protein S14 (MRPS14, Accession NM_022100). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS14. LOC91351 (Accession XM_037817) is another VGAM1286 host target gene. LOC91351 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91351 BINDING SITE, designated SEQ ID:32695, to the nucleotide sequence of VGAM1286 RNA, herein designated VGAM RNA, also designated SEQ ID:3997.

[45694] Another function of VGAM1286 is therefore inhibition of LOC91351 (Accession XM_037817). Accordingly, utilities of VGAM1286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91351. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1287 (VGAM1287) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45695] VGAM1287 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1287 was detected is described hereinabove with reference to Figs. 1-8.

[45696] VGAM1287 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Beet Virus Q. VGAM1287 host target gene, herein designated VGAM HOST TARGET

GENE, is a human gene contained in the human genome.

[45697] VGAM1287 gene encodes a VGAM1287 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1287 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1287 precursor RNA is designated SEQ ID:1273, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1273 is located at position 1305 relative to the genome of Beet Virus Q.

[45698] VGAM1287 precursor RNA folds onto itself, forming VGAM1287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45699] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1287 folded precursor RNA into VGAM1287 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1287 RNA is designated SEQ ID:3998, and is provided hereinbelow with reference to the sequence listing part.

[45700] VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1287 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45701] VGAM1287 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1287 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1287 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45702] The complementary binding of VGAM1287 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1287 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1287 host target RNA into VGAM1287 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45703] It is appreciated that VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1287 host target genes. The mRNA of each one of this plurality of VGAM1287 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1287 RNA, herein designated VGAM RNA, and which when bound by VGAM1287 RNA causes inhibition of translation of respective one or more VGAM1287 host target proteins.

[45704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1287 gene, herein designated VGAM GENE, on one or more VGAM1287 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45705] It is yet further appreciated that a function of VGAM1287 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities, of VGAM1287 correlate with, and may be deduced from, the identity of the host target genes which VGAM1287 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45706] Nucleotide sequences of the VGAM1287 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1287 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1287 are further described hereinbelow with reference to Table 1.

[45707] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1287 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1287 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45708] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1287 gene, herein designated VGAM is inhibition of expression of VGAM1287 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1287 correlate with, and may be deduced from, the identity of the target genes which VGAM1287 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45709] ATPase, Cu⁺⁺ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM_000052) is a VGAM1287 host target gene. ATP7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7A BINDING SITE, designated SEQ ID:5492, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:3998.

[45710] A function of VGAM1287 is therefore inhibition of ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM_000052). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7A. CGTHBA (Accession NM_012075) is another VGAM1287 host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14355, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45711] Another function of VGAM1287 is therefore inhibition of CGTHBA (Accession NM_012075). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Estrogen-related Receptor Gamma (ESRRG, Accession XM_039053) is another VGAM1287 host target gene. ESRRG BINDING SITE is HOST TARGET binding site

found in the 3` untranslated region of mRNA encoded by ESRRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESRRG BINDING SITE, designated SEQ ID:32997, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45712] Another function of VGAM1287 is therefore inhibition of Estrogen-related Receptor Gamma (ESRRG, Accession XM_039053), a gene which Estrogen-related receptor gamma. Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESRRG. The function of ESRRG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM359.Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449) is another VGAM1287 host target gene. RFX5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6045, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45713] Another function of VGAM1287 is therefore inhibition of Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449), a gene which activates transcription from class ii mhc promoters. Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169) is another VGAM1287 host target gene. SUFU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUFU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUFU BINDING SITE, designated SEQ ID:18251, to the nucleotide sequence of

VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45714] Another function of VGAM1287 is therefore inhibition of Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUFU. DJ971N18.2 (Accession NM_021156) is another VGAM1287 host target gene. DJ971N18.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ971N18.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ971N18.2 BINDING SITE, designated SEQ ID:22133, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45715] Another function of VGAM1287 is therefore inhibition of DJ971N18.2 (Accession NM_021156). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ971N18.2. FLJ20079 (Accession NM_017656) is another VGAM1287 host target gene. FLJ20079 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19170, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45716] Another function of VGAM1287 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. KIAA1949 (Accession XM_175173) is another VGAM1287 host target gene. KIAA1949 BINDING SITE1 through KIAA1949 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1949, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1949 BINDING SITE1 through KIAA1949 BINDING SITE3, designated SEQ ID:46667, SEQ ID:44208 and SEQ ID:46712 respectively, to the nucleotide sequence of VGAM1287 RNA, herein designated

VGAM RNA, also designated SEQ ID:3998.

[45717] Another function of VGAM1287 is therefore inhibition of KIAA1949 (Accession XM_175173). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1949. Testis-specific Transcript, Y-linked 2 (TTY2, Accession XM_099029) is another VGAM1287 host target gene. TTY2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TTY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY2 BINDING SITE, designated SEQ ID:42070, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45718] Another function of VGAM1287 is therefore inhibition of Testis-specific Transcript, Y-linked 2 (TTY2, Accession XM_099029). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY2. LOC159148 (Accession XM_099030) is another VGAM1287 host target gene. LOC159148 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by LOC159148, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159148 BINDING SITE, designated SEQ ID:42077, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45719] Another function of VGAM1287 is therefore inhibition of LOC159148 (Accession XM_099030). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159148. LOC199692 (Accession NM_145295) is another VGAM1287 host target gene. LOC199692 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC199692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199692 BINDING SITE, designated SEQ ID:29810, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45720] Another function of VGAM1287 is therefore inhibition of

LOC199692 (Accession NM_145295). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199692. LOC91012 (Accession XM_035503) is another VGAM1287 host target gene. LOC91012 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91012 BINDING SITE, designated SEQ ID:32280, to the nucleotide sequence of VGAM1287 RNA, herein designated VGAM RNA, also designated SEQ ID:3998.

[45721] Another function of VGAM1287 is therefore inhibition of LOC91012 (Accession XM_035503). Accordingly, utilities of VGAM1287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91012. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1288 (VGAM1288) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[45722] VGAM1288 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1288 was detected is described hereinabove with reference to Figs. 1–8.

[45723] VGAM1288 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45724] VGAM1288 gene encodes a VGAM1288 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1288 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1288 precursor RNA is designated SEQ ID:1274, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1274 is located at position 9116 relative to the genome of Saimiriine Herpesvirus 2.

[45725] VGAM1288 precursor RNA folds onto itself, forming VGAM1288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45726] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1288 folded precursor RNA into VGAM1288 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1288 RNA is designated SEQ ID:3999, and is provided hereinbelow with reference to the sequence listing part.

[45727] VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1288 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[45728] VGAM1288 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1288 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1288 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[45729] The complementary binding of VGAM1288 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1288 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1288 host target RNA into VGAM1288 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45730] It is appreciated that VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1288 host target genes. The mRNA of each one of this plurality of VGAM1288 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1288 RNA, herein designated VGAM RNA, and which when bound by VGAM1288 RNA causes inhibition of translation of respective one or more VGAM1288 host target proteins.

[45731] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1288 gene, herein designated VGAM GENE, on one

or more VGAM1288 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45732] It is yet further appreciated that a function of VGAM1288 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1288 correlate with, and may be deduced from, the identity of the host target genes which VGAM1288 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45733] Nucleotide sequences of the VGAM1288 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1288 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1288 are further described hereinbelow with reference to Table 1.

[45734] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1288 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1288 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45735] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1288 gene, herein designated VGAM is inhibition of expression of VGAM1288 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1288 correlate with, and may be deduced from, the identity of the target genes which VGAM1288 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45736] Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase)

(FUT6, Accession NM_000150) is a VGAM1288 host target gene. FUT6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FUT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT6 BINDING SITE, designated SEQ ID:5649, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45737] A function of VGAM1288 is therefore inhibition of Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM_000150), a gene which is involved in the biosynthesis of the e-selectin ligand, sialyl-lewis x. catalyzes the transfer of fucose from gdp- beta-fucose to alpha-2,3 sialylated substrates. Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT6. The function of FUT6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM194. Protein Kinase C, Nu (PRKCN, Accession NM_005813) is another VGAM1288 host target gene. PRKCN BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12399, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45738] Another function of VGAM1288 is therefore inhibition of Protein Kinase C, Nu (PRKCN, Accession NM_005813). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCN. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 2 (SMARCD2, Accession NM_003077) is another VGAM1288 host target gene. SMARCD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMARCD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD2 BINDING SITE, designated SEQ ID:9052, to the nucleotide sequence of VGAM1288 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3999.

[45739] Another function of VGAM1288 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 2 (SMARCD2, Accession NM_003077), a gene which is involved in chromatin remodeling. Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD2. The function of SMARCD2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM554. Surfeit 5 (SURF5, Accession NM_006752) is another VGAM1288 host target gene. SURF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SURF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SURF5 BINDING SITE, designated SEQ ID:13605, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45740] Another function of VGAM1288 is therefore inhibition of

Surfeit 5 (SURF5, Accession NM_006752). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SURF5. FLJ11142 (Accession NM_018338) is another VGAM1288 host target gene. FLJ11142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11142 BINDING SITE, designated SEQ ID:20342, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45741] Another function of VGAM1288 is therefore inhibition of FLJ11142 (Accession NM_018338). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11142. KIAA0256 (Accession XM_034905) is another VGAM1288 host target gene. KIAA0256 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0256, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0256 BINDING SITE, designated SEQ ID:32186, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45742] Another function of VGAM1288 is therefore inhibition of KIAA0256 (Accession XM_034905). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0256. KIAA1450 (Accession XM_038035) is another VGAM1288 host target gene. KIAA1450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1450 BINDING SITE, designated SEQ ID:32748, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45743] Another function of VGAM1288 is therefore inhibition of KIAA1450 (Accession XM_038035). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1450. KIAA1829 (Accession XM_030378) is another

VGAM1288 host target gene. KIAA1829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1829 BINDING SITE, designated SEQ ID:31032, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45744] Another function of VGAM1288 is therefore inhibition of KIAA1829 (Accession XM_030378). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1829. PRO1580 (Accession NM_018502) is another VGAM1288 host target gene. PRO1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1580 BINDING SITE, designated SEQ ID:20566, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45745] Another function of VGAM1288 is therefore inhibition of PRO1580 (Accession NM_018502). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1580. LOC149373 (Accession XM_086507) is another VGAM1288 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38718, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45746] Another function of VGAM1288 is therefore inhibition of LOC149373 (Accession XM_086507). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC165246 (Accession XM_092473) is another VGAM1288 host target gene. LOC165246 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165246, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165246 BINDING SITE, designated SEQ ID:40126, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45747] Another function of VGAM1288 is therefore inhibition of LOC165246 (Accession XM_092473). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165246. LOC256207 (Accession XM_170837) is another VGAM1288 host target gene. LOC256207 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256207, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256207 BINDING SITE, designated SEQ ID:45620, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45748] Another function of VGAM1288 is therefore inhibition of LOC256207 (Accession XM_170837). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC256207. LOC90459 (Accession XM_031826) is another VGAM1288 host target gene. LOC90459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90459 BINDING SITE, designated SEQ ID:31489, to the nucleotide sequence of VGAM1288 RNA, herein designated VGAM RNA, also designated SEQ ID:3999.

[45749] Another function of VGAM1288 is therefore inhibition of LOC90459 (Accession XM_031826). Accordingly, utilities of VGAM1288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90459. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1289 (VGAM1289) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45750] VGAM1289 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1289 was detected is described hereinabove with reference to Figs. 1–8.

[45751] VGAM1289 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45752] VGAM1289 gene encodes a VGAM1289 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1289 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1289 precursor RNA is designated SEQ ID:1275, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1275 is located at position 9692 relative to the genome of Saimiriine Herpesvirus 2.

[45753] VGAM1289 precursor RNA folds onto itself, forming VGAM1289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45754] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1289 folded precursor RNA into VGAM1289 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1289 RNA is designated SEQ ID:4000, and is provided hereinbelow with reference to the sequence listing part.

[45755] VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1289 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45756] VGAM1289 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1289 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1289 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45757] The complementary binding of VGAM1289 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1289 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1289 host target RNA into VGAM1289 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45758] It is appreciated that VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1289 host target genes. The mRNA of each one of this plurality of VGAM1289 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1289 RNA, herein designated VGAM RNA, and which when bound by VGAM1289 RNA causes inhibition of translation of respective one or more VGAM1289 host target proteins.

[45759] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1289 gene, herein designated VGAM GENE, on one or more VGAM1289 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45760] It is yet further appreciated that a function of VGAM1289 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1289 correlate with, and may be deduced from, the identity of the host target genes which VGAM1289 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45761] Nucleotide sequences of the VGAM1289 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1289 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1289 are further described hereinbelow with reference to Table 1.

[45762] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1289 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1289 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45763] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1289 gene, herein designated VGAM is inhibition of expression of VGAM1289 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1289 correlate with, and may be deduced from, the identity of the target genes which VGAM1289 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45764] Cyclin D2 (CCND2, Accession NM_001759) is a VGAM1289 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7513, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45765] A function of VGAM1289 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the g1/s (start) transition. Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. EphA2 (EPHA2, Accession NM_004431) is another VGAM1289 host target gene. EPHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA2 BINDING SITE, designated SEQ ID:10714, to the nucleotide se-

quence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45766] Another function of VGAM1289 is therefore inhibition of EphA2 (EPHA2, Accession NM_004431), a gene which binds to ephrin-a1, -a3, -a4 and -a5. Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA2. The function of EPHA2 has been established by previous studies. See 179610 for background on Eph receptors and their ligands, the ephrins. By screening a HeLa cell cDNA library with degenerate oligonucleotides based on highly conserved regions of receptor protein-tyrosine kinases, Lindberg and Hunter (1990) isolated cDNAs encoding EPHA2, named ECK by them. The predicted 976-amino acid protein consists of a 534-amino acid external domain that includes a signal peptide; a 24-amino acid transmembrane domain; and a 418-amino acid cytoplasmic domain that contains a canonical protein-tyrosine kinase catalytic domain. Immunoprecipitated ECK from human cells migrated as an approximately 125- to 130-kD doublet by SDS-PAGE. Northern blot analysis detected an approximately 4.7-kb ECK transcript in human cells. Rat ECK mRNA is highly expressed in tissues that

contain a high proportion of epithelial cells, including lung, skin, small intestine, and ovary. Immunohistochemical analysis detected rat Eck protein in lung and kidney epithelial cells. By somatic cell hybrid analysis and fluorescence in situ hybridization, Sulman et al. (1997) mapped the EPHA2 gene, called ECK by them, to 1p36.1. They noted that there appears to be clusters of EPH genes on several chromosomes. Ganju et al. (1994) mapped the mouse Eck gene to the distal region of chromosome 4, between the Akp2 (OMIM Ref. No. 171760) and Gpd1 (OMIM Ref. No. 138420) genes. They noted that this region shows homology of synteny with human 1p36-p34.

[45767] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45768] Lindberg, R. A.; Hunter, T. : cDNA cloning and characterization of eck, an epithelial cell receptor-tyrosine kinase in the eph/elk family of protein kinases. Molec. Cell. Biol. 10: 6316-6324, 1990. ; and

[45769] Sulman, E. P.; Tang, X. X.; Allen, C.; Biegel, J. A.; Pleasure, D. E.; Brodeur, G. M.; Ikegaki, N. : ECK, a human EPH-related gene, maps to 1p36.1, a common region of alteration in human.

[45770] Further studies establishing the function and utilities of EPHA2 are found in John Hopkins OMIM database record ID 176946, and in cited publications numbered 12702–12704 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788) is another VGAM1289 host target gene. UBE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4A BINDING SITE, designated SEQ ID:11197, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45771] Another function of VGAM1289 is therefore inhibition of Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788), a gene which binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with UBE4A. The function of UBE4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60.DKFZP434P0721 (Accession XM_033181) is another VGAM1289 host target gene. DKFZP434P0721 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434P0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0721 BINDING SITE, designated SEQ ID:31874, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45772] Another function of VGAM1289 is therefore inhibition of DKFZP434P0721 (Accession XM_033181). Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0721. FLJ10287 (Accession NM_019083) is another VGAM1289 host target gene. FLJ10287 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10287, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10287 BINDING SITE, designated SEQ ID:21155, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45773] Another function of VGAM1289 is therefore inhibition of FLJ10287 (Accession NM_019083). Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10287. FLJ10607 (Accession XM_085119) is another VGAM1289 host target gene. FLJ10607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10607 BINDING SITE, designated SEQ ID:37835, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45774] Another function of VGAM1289 is therefore inhibition of FLJ10607 (Accession XM_085119). Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ10607. KIAA0182 (Accession XM_050495) is another VGAM1289 host target gene. KIAA0182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0182 BINDING SITE, designated SEQ ID:35646, to the nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45775] Another function of VGAM1289 is therefore inhibition of KIAA0182 (Accession XM_050495). Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0182. KIAA1908 (Accession XM_055834) is another VGAM1289 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36327, to the

nucleotide sequence of VGAM1289 RNA, herein designated VGAM RNA, also designated SEQ ID:4000.

[45776] Another function of VGAM1289 is therefore inhibition of KIAA1908 (Accession XM_055834). Accordingly, utilities of VGAM1289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1290 (VGAM1290) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45777] VGAM1290 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1290 was detected is described hereinabove with reference to Figs. 1–8.

[45778] VGAM1290 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Grapevine Fleck Virus. VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45779] VGAM1290 gene encodes a VGAM1290 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1290 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1290 precursor RNA is designated SEQ ID:1276, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1276 is located at position 5505 relative to the genome of Grapevine Fleck Virus.

[45780] VGAM1290 precursor RNA folds onto itself, forming VGAM1290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45781] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1290 folded precursor RNA into VGAM1290 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1290 RNA is designated SEQ ID:4001, and is provided hereinbelow with reference to the sequence listing part.

[45782] VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1290 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45783] VGAM1290 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1290 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1290 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45784] The complementary binding of VGAM1290 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1290 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1290 host target RNA into VGAM1290 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45785] It is appreciated that VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1290 host target genes. The mRNA of each one of this plurality of VGAM1290 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1290 RNA, herein designated VGAM RNA, and which when bound by VGAM1290 RNA causes inhibition of translation of respective one or more VGAM1290 host target proteins.

[45786] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1290 gene, herein designated VGAM GENE, on one or more VGAM1290 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[45787] It is yet further appreciated that a function of VGAM1290 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of viral infection by Grapevine Fleck Virus. Specific functions, and accordingly utilities, of VGAM1290 correlate with, and may be deduced from, the identity of the host target genes which VGAM1290 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45788] Nucleotide sequences of the VGAM1290 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1290 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1290 are further described hereinbelow with reference to Table 1.

[45789] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1290 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1290 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45790] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1290 gene, herein designated VGAM is inhibition of expression of VGAM1290 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1290 correlate with, and may be deduced from, the identity of the target genes which VGAM1290 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45791] Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM_001174) is a VGAM1290 host target gene. ARHGAP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP6 BINDING SITE, designated SEQ ID:6844, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45792] A function of VGAM1290 is therefore inhibition of Rho

GTPase Activating Protein 6 (ARHGAP6, Accession NM_001174), a gene which activates the rho-type GTPases by converting them to an inactive GTP-bound state. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP6. The function of ARHGAP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Cathepsin B (CTSB, Accession XM_035662) is another VGAM1290 host target gene. CTSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTSB BINDING SITE, designated SEQ ID:32327, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45793] Another function of VGAM1290 is therefore inhibition of Cathepsin B (CTSB, Accession XM_035662). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CTSB. Dystrophin Myotonic-protein Kinase (DMPK, Accession NM_004409) is another VGAM1290 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10661, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45794] Another function of VGAM1290 is therefore inhibition of Dystrophin Myotonic-protein Kinase (DMPK, Accession NM_004409). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. DNA (cytosine-5-)-methyltransferase 3-like (DNMT3L, Accession NM_013369) is another VGAM1290 host target gene. DNMT3L BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DNMT3L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3L BINDING SITE, designated SEQ

ID:15017, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45795] Another function of VGAM1290 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 3-like (DNMT3L, Accession NM_013369), a gene which plays a role in de novo methylation of CpG islands. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3L. The function of DNMT3L and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM447. Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055) is another VGAM1290 host target gene. GFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFAP BINDING SITE, designated SEQ ID:7812, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45796] Another function of VGAM1290 is therefore inhibition of

Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFAP. Mucin 3B (MUC3B, Accession XM_168578) is another VGAM1290 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ ID:45252, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45797] Another function of VGAM1290 is therefore inhibition of Mucin 3B (MUC3B, Accession XM_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM55. Mucin 4, Tracheobronchial (MUC4, Accession NM_138298) is another VGAM1290 host target gene. MUC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MUC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC4 BINDING SITE, designated SEQ ID:28710, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45798] Another function of VGAM1290 is therefore inhibition of Mucin 4, Tracheobronchial (MUC4, Accession NM_138298), a gene which may act as a ligand for ErbB2 mediated cell signalling. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC4. The function of MUC4 has been established by previous studies. From a lambda-gt11 cDNA library constructed from human tracheobronchial mucosa, Porchet et al. (1991) isolated a partial cDNA clone that reacted with a polyclonal antiserum raised to chemically deglycosylated pronase glycopeptides from human bronchial mucins. The

novel tracheobronchial mucin gene, referred to as mucin 4, was mapped to chromosome 3 by analysis of somatic cell hybrids. By in situ hybridization, Van Cong et al. (1991) mapped MUC4 to 3q29. They also demonstrated a VNTR polymorphism useful for family linkage studies. The full report was given by Gross et al. (1992). (Note that Nguyen Van Cong's name is sometimes published as Nguyen, V. C. rather than Van Cong, N. Nguyen is indeed the surname.)

[45799] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45800] Gross, M.-S.; Guyonnet-Duperat, V.; Porchet, N.; Bernheim, A.; Aubert, J. P.; Nguyen, V. C. : Mucin 4 (MUC4) gene: regional assignment (3q29) and RFLP analysis. Ann. Genet. 35: 21-26, 1992. ; and

[45801] Porchet, N.; Van Cong, N.; Dufosse, J.; Audie, J. P.; Guyonnet-Duperat, V.; Gross, M. S.; Denis, C.; Degand, P.; Bernheim, A.; Aubert, J. P. : Molecular cloning and chromosomal localization.

[45802] Further studies establishing the function and utilities of MUC4 are found in John Hopkins OMIM database record ID 158372, and in cited publications numbered 3797-3799

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rhodopsin (opsin 2, rod pigment) (retinitis pigmentosa 4, autosomal dominant) (RHO, Accession NM_000539) is another VGAM1290 host target gene. RHO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHO BINDING SITE, designated SEQ ID:6138, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45803] Another function of VGAM1290 is therefore inhibition of Rhodopsin (opsin 2, rod pigment) (retinitis pigmentosa 4, autosomal dominant) (RHO, Accession NM_000539). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHO. X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM_005432) is another VGAM1290 host target gene. XRCC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

XRCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC3 BINDING SITE, designated SEQ ID:11907, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45804] Another function of VGAM1290 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM_005432), a gene which is required for meiotic recombination, synaptonemal complex formation and cell cycle progression. Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC3. The function of XRCC3 has been established by previous studies. Masson et al. (2001) found that antibody directed against RAD51C (OMIM Ref. No. 602774) coimmunoprecipitated XRCC2 in an endogenous complex with RAD51C in HeLa cell lysates. Gel filtration of the complex suggested that a heterodimer is formed between the proteins. Using coprecipitation and multiple pull-down assays, Liu et al. (2002) confirmed interaction between these proteins. They also found that

RAD51 coprecipitates with XRCC3, suggesting that RAD51 can be present in a trimeric complex of XRCC3, RAD51C, and RAD51. Brenneman et al. (2002) found that XRCC3 mutant cells displayed radically altered homologous recombination (HR) product spectra, with increased gene conversion tract lengths, increased frequencies of discontinuous tracts, and frequent local rearrangements associated with HR. These results indicated that XRCC3 function is not limited to HR initiation, but extends to later stages in formation and resolution of HR intermediates, possibly by stabilizing heteroduplex DNA. The results further demonstrated that HR defects can promote genomic instability not only through failure to initiate HR (leading to nonhomologous repair), but also through aberrant processing of HR intermediates. The authors suggested that both mechanisms may contribute to carcinogenesis in HR-deficient cells.

[45805] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45806] Masson, J.-Y.; Tarsounas, M. C.; Stasiak, A. Z.; Stasiak, A.; Shah, R.; McIlwraith, M. J.; Benson, F. E.; West, S. C. : Identification and purification of two distinct complexes con-

taining the five RAD51 paralogs. Genes Dev. 15:
3296–3307, 2001. ; and

[45807] Brenneman, M. A.; Wagener, B. M.; Miller, C. A.; Allen, C.; Nickoloff, J. A. : XRCC3 controls the fidelity of homologous recombination: roles for XRCC3 in late stages of recombination.

[45808] Further studies establishing the function and utilities of XRCC3 are found in John Hopkins OMIM database record ID 600675, and in cited publications numbered 9920–9921, 1602–160 and 9922–9923 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Docking Protein 4 (DOK4, Accession NM_018110) is another VGAM1290 host target gene. DOK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOK4 BINDING SITE, designated SEQ ID:19880, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45809] Another function of VGAM1290 is therefore inhibition of Docking Protein 4 (DOK4, Accession NM_018110). Ac-

cordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOK4. FLJ12910 (Accession NM_024573) is another VGAM1290 host target gene. FLJ12910 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12910 BINDING SITE, designated SEQ ID:23799, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45810] Another function of VGAM1290 is therefore inhibition of FLJ12910 (Accession NM_024573). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12910. KIAA1130 (Accession XM_031104) is another VGAM1290 host target gene. KIAA1130 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1130 BINDING SITE, designated SEQ ID:31282, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45811] Another function of VGAM1290 is therefore inhibition of KIAA1130 (Accession XM_031104). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1130. KIAA1297 (Accession XM_051005) is another VGAM1290 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35709, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45812] Another function of VGAM1290 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. N-myristoyltransferase 1 (NMT1, Accession NM_021079) is another VGAM1290 host target gene.

NMT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NMT1 BINDING SITE, designated SEQ ID:22048, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45813] Another function of VGAM1290 is therefore inhibition of N-myristoyltransferase 1 (NMT1, Accession NM_021079). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NMT1. Phosphatase, Orphan 1 (phospho1, Accession XM_091572) is another VGAM1290 host target gene. phospho1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by phospho1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of phospho1 BINDING SITE, designated SEQ ID:40060, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45814] Another function of VGAM1290 is therefore inhibition of Phosphatase, Orphan 1 (phospho1, Accession XM_091572). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with phospho1. LOC149606 (Accession XM_086600) is another VGAM1290 host target gene. LOC149606 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149606, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149606 BINDING SITE, designated SEQ ID:38781, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45815] Another function of VGAM1290 is therefore inhibition of LOC149606 (Accession XM_086600). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149606. LOC206426 (Accession XM_116505) is another VGAM1290 host target gene. LOC206426 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC206426, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206426 BINDING SITE, designated SEQ ID:43117, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45816] Another function of VGAM1290 is therefore inhibition of LOC206426 (Accession XM_116505). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206426. LOC221486 (Accession XM_165760) is another VGAM1290 host target gene. LOC221486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221486 BINDING SITE, designated SEQ ID:43741, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45817] Another function of VGAM1290 is therefore inhibition of LOC221486 (Accession XM_165760). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC221486. LOC91208 (Accession XM_036935) is another VGAM1290 host target gene. LOC91208 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91208, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91208 BINDING SITE, designated SEQ ID:32522, to the nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45818] Another function of VGAM1290 is therefore inhibition of LOC91208 (Accession XM_036935). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91208. LOC93589 (Accession XM_052387) is another VGAM1290 host target gene. LOC93589 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC93589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93589 BINDING SITE, designated SEQ ID:35977, to the

nucleotide sequence of VGAM1290 RNA, herein designated VGAM RNA, also designated SEQ ID:4001.

[45819] Another function of VGAM1290 is therefore inhibition of LOC93589 (Accession XM_052387). Accordingly, utilities of VGAM1290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93589. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1291 (VGAM1291) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45820] VGAM1291 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1291 was detected is described hereinabove with reference to Figs. 1–8.

[45821] VGAM1291 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox Virus.

VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45822] VGAM1291 gene encodes a VGAM1291 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1291 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1291 precursor RNA is designated SEQ ID:1277, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1277 is located at position 74471 relative to the genome of Swinepox Virus.

[45823] VGAM1291 precursor RNA folds onto itself, forming VGAM1291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45824] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1291 folded precursor RNA into VGAM1291 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1291 RNA is designated SEQ ID:4002, and is provided hereinbelow with reference to the sequence listing part.

[45825] VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1291 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45826] VGAM1291 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1291 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1291 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45827] The complementary binding of VGAM1291 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1291 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1291 host target RNA into VGAM1291 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45828] It is appreciated that VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1291 host target genes. The mRNA of each one of this plurality of VGAM1291 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1291 RNA, herein designated VGAM RNA, and which when bound by VGAM1291 RNA causes inhibition of translation of respective one or more VGAM1291 host target proteins.

[45829] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1291 gene, herein designated VGAM GENE, on one or more VGAM1291 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[45830] It is yet further appreciated that a function of VGAM1291 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of viral infection by Swinepox Virus. Specific functions, and accordingly utilities, of VGAM1291 correlate with, and may be deduced from, the identity of the host target genes which VGAM1291 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45831] Nucleotide sequences of the VGAM1291 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1291 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1291 are further described hereinbelow with reference to Table 1.

[45832] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1291 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1291 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45833] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1291 gene, herein designated VGAM is inhibition of expression of VGAM1291 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1291 correlate with, and may be deduced from, the identity of the target genes which VGAM1291 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45834] Interleukin-1 Receptor-associated Kinase 4 (IRAK4, Accession XM_028349) is a VGAM1291 host target gene. IRAK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRAK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRAK4 BINDING SITE, designated SEQ ID:30693, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45835] A function of VGAM1291 is therefore inhibition of Inter-

leukin-1 Receptor-associated Kinase 4 (IRAK4, Accession XM_028349), a gene which may function as an IRAK1 kinase, triggering a cascade of phosphorylation events. Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK4. The function of IRAK4 has been established by previous studies. By SEREX (serologic analysis of recombinant cDNA expression libraries) screening of renal tumors, Scanlan et al. (1999) identified multiple antigens, including REN64. The deduced 460-amino acid protein is strongly expressed in kidney, as determined by immunohistochemistry. RT-PCR analysis detected expression in all 6 tissues tested (lung, testis, small intestine, breast, liver, and placenta). By database searching for IRAK-like sequences and PCR of a universal cDNA library, Li et al. (2002) obtained a cDNA encoding IRAK4, which is 98% identical to REN64. The predicted protein is 84% identical to the mouse protein and, like IRAK1, IRAK2 (OMIM Ref. No. 603304), IRAKM (OMIM Ref. No. 604459), and the Drosophila Pelle protein, it has an N-terminal death domain and a central kinase domain. Unlike the other IRAK proteins, however, but similar to Pelle, IRAK4 has a short C-terminal domain. Northern blot analysis re-

vealed expression of 3.0- and 4.4-kb transcripts, with strongest expression in kidney and liver. RT-PCR analysis detected wide, low-level expression of IRAK4. Functional analysis by Li et al. (2002) determined that IRAK4, like IRAK1 and Pelle, has auto- and cross-phosphorylation kinase activity. Precipitation and binding analyses showed weak interaction between IRAK4 and IRAK1, but IRAK4 did not interact with other IRAK family members. Overexpressed IRAK4 interacted with MYD88 (OMIM Ref. No. 602170) and TRAF6 (OMIM Ref. No. 602355) and activated mitogen-activated protein kinase (MAPK) and nuclear factor kappa-B (NFKB; 164011) pathways. Endogenous IRAK4 associated in a transient IL1 (see OMIM Ref. No. 147720)-dependent manner with unmodified IRAK1 and TRAF6. Luciferase reporter analysis showed that IRAK4 lacking the kinase domain inhibited IL1- but not tumor necrosis factor (TNF; 191160)- induced NFKB and IRAK1 activation. SDS-PAGE and autoradiographic analysis indicated that IRAK4 phosphorylates and activates IRAK1 at thr387, but not vice versa. Li et al. (2002) proposed that IRAK4 acts upstream of other IRAKs and may function as an IRAK1 kinase, triggering a cascade of phosphorylation events By gene targeting, Suzuki et al. (2002) generated

mice deficient in Irak4. Mutant mice and macrophages or embryonic fibroblasts (MEFs) from these mice were unable to respond to Il1 by production of Il6 (OMIM Ref. No. 147620), Tnf, or nitric oxide, or by activation of Nfkb or Jnk (OMIM Ref. No. 601158). Responses to Tnf, however, were intact, suggesting that the defect was specific for Il1. Analysis of responses to lipopolysaccharide (LPS), bacterial DNA (unmethylated CpG), peptidoglycan, or viral RNA extended the importance of Irak4 to Tlr4, Tlr9 (OMIM Ref. No. 605474), Tlr2 (OMIM Ref. No. 603028), and Tlr3 (OMIM Ref. No. 603029), respectively, which use signaling mechanisms similar to IL1R. Challenge of Irak4 $-/-$ mice with lymphocytic choriomeningitis virus showed reduced production of gamma-interferon (IFNG; 147570) by natural killer cells, but no loss of cytolytic function of these cells. Challenge with Staphylococcus aureus was lethal in all mutant mice but not in most wildtype mice. Luciferase reporter analysis suggested that Irak4 acts upstream of Myd88 and Mal (OMIM Ref. No. 606252) and downstream of Traf6. Animal model experiments lend further support to the function of IRAK4. By gene targeting, Suzuki et al. (2002) generated mice deficient in Irak4. Mutant mice and macrophages or embryonic fibroblasts (MEFs) from these

mice were unable to respond to Il1 by production of Il6 (OMIM Ref. No. 147620), Tnf, or nitric oxide, or by activation of Nfkb or Jnk (OMIM Ref. No. 601158). Responses to Tnf, however, were intact, suggesting that the defect was specific for Il1. Analysis of responses to lipopolysaccharide (LPS), bacterial DNA (unmethylated CpG), peptidoglycan, or viral RNA extended the importance of Irak4 to Tlr4, Tlr9 (OMIM Ref. No. 605474), Tlr2 (OMIM Ref. No. 603028), and Tlr3 (OMIM Ref. No. 603029), respectively, which use signaling mechanisms similar to IL1R. Challenge of Irak4 $-/-$ mice with lymphocytic choriomeningitis virus showed reduced production of gamma-interferon (IFNG; 147570) by natural killer cells, but no loss of cytolytic function of these cells. Challenge with *Staphylococcus aureus* was lethal in all mutant mice but not in most wildtype mice. Luciferase reporter analysis suggested that Irak4 acts upstream of Myd88 and Mal (OMIM Ref. No. 606252) and downstream of Traf6

[45836] It is appreciated that the abovementioned animal model for IRAK4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[45837] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

[45838] Li, S.; Strelow, A.; Fontana, E. J.; Wesche, H. : IRAK-4: a novel member of the IRAK family with the properties of an IRAK-kinase. Proc. Nat. Acad. Sci. 99: 5567-5572, 2002. ; and

[45839] Scanlan, M. J.; Gordon, J. D.; Williamson, B.; Stockert, E.; Bander, N. H.; Jongeneel, V.; Gure, A. O.; Jager, D.; Jager, E.; Knuth, A.; Chen, Y.-T.; Old, L. J. : Antigens recognized b.

[45840] Further studies establishing the function and utilities of IRAK4 are found in John Hopkins OMIM database record ID 606883, and in cited publications numbered 6391-6394 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ20772

(Accession NM_017956) is another VGAM1291 host target gene. FLJ20772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20772 BINDING SITE, designated SEQ ID:19664, to the nucleotide sequence of VGAM1291

RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45841] Another function of VGAM1291 is therefore inhibition of FLJ20772 (Accession NM_017956). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20772. Vav 3 Oncogene (VAV3, Accession NM_006113) is another VGAM1291 host target gene. VAV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VAV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAV3 BINDING SITE, designated SEQ ID:12758, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45842] Another function of VGAM1291 is therefore inhibition of Vav 3 Oncogene (VAV3, Accession NM_006113). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAV3. LOC150759 (Accession XM_086995) is another VGAM1291 host target gene. LOC150759 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC150759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150759 BINDING SITE, designated SEQ ID:39013, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45843] Another function of VGAM1291 is therefore inhibition of LOC150759 (Accession XM_086995). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150759. LOC151323 (Accession XM_087168) is another VGAM1291 host target gene. LOC151323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151323 BINDING SITE, designated SEQ ID:39102, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45844] Another function of VGAM1291 is therefore inhibition of LOC151323 (Accession XM_087168). Accordingly, utilities

of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151323. LOC200399 (Accession XM_114226) is another VGAM1291 host target gene. LOC200399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200399 BINDING SITE, designated SEQ ID:42810, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45845] Another function of VGAM1291 is therefore inhibition of LOC200399 (Accession XM_114226). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200399. LOC253955 (Accession XM_170486) is another VGAM1291 host target gene. LOC253955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC253955 BINDING SITE, designated SEQ ID:45325, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45846] Another function of VGAM1291 is therefore inhibition of LOC253955 (Accession XM_170486). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253955. LOC91923 (Accession XM_041526) is another VGAM1291 host target gene. LOC91923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91923 BINDING SITE, designated SEQ ID:33543, to the nucleotide sequence of VGAM1291 RNA, herein designated VGAM RNA, also designated SEQ ID:4002.

[45847] Another function of VGAM1291 is therefore inhibition of LOC91923 (Accession XM_041526). Accordingly, utilities of VGAM1291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91923. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1292 (VGAM1292) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45848] VGAM1292 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1292 was detected is described hereinabove with reference to Figs. 1–8.

[45849] VGAM1292 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Swinepox Virus. VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45850] VGAM1292 gene encodes a VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1292 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1292 precursor RNA is designated SEQ ID:1278, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1278 is located at position 74650 relative to the

genome of Swinepox Virus.

[45851] VGAM1292 precursor RNA folds onto itself, forming VGAM1292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45852] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1292 folded precursor RNA into VGAM1292 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1292 RNA is designated SEQ ID:4003, and is provided hereinbelow with reference to the sequence listing part.

[45853] VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1292 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45854] VGAM1292 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1292 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1292 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45855] The complementary binding of VGAM1292 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1292 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1292 host target RNA into VGAM1292 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45856] It is appreciated that VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1292 host target genes. The mRNA of each one of this plurality of VGAM1292 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1292 RNA, herein designated VGAM RNA, and which when bound by VGAM1292 RNA causes inhibition of translation of respective one or more VGAM1292 host target proteins.

[45857] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1292 gene, herein designated VGAM GENE, on one or more VGAM1292 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45858] It is yet further appreciated that a function of VGAM1292 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1292 include diagnosis, prevention and treatment of viral infection by Swinepox Virus. Specific functions, and accordingly utilities, of VGAM1292 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1292 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45859] Nucleotide sequences of the VGAM1292 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1292 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1292 are further described hereinbelow with reference to Table 1.

[45860] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1292 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1292 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45861] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1292 gene, herein designated VGAM is inhibition of expression of VGAM1292 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1292 correlate with, and may be deduced

from, the identity of the target genes which VGAM1292 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45862] G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776) is a VGAM1292 host target gene. GIT2 BINDING SITE1 through GIT2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GIT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE1 through GIT2 BINDING SITE3, designated SEQ ID:16596, SEQ ID:27678 and SEQ ID:27691 respectively, to the nucleotide sequence of VGAM1292 RNA, herein designated VGAM RNA, also designated SEQ ID:4003.

[45863] A function of VGAM1292 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_014776). Accordingly, utilities of VGAM1292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. DRCTNNB1A (Accession NM_032581) is another VGAM1293 host target gene. DRCTNNB1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by DRCTNNB1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRCTNNB1A BINDING SITE, designated SEQ ID:26314, to the nucleotide sequence of VGAM1293 RNA, herein designated VGAM RNA, also designated SEQ ID:4004.

[45864] Another function of VGAM1293 is therefore inhibition of DRCTNNB1A (Accession NM_032581). Accordingly, utilities of VGAM1293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRCTNNB1A. HGC6.1.1 (Accession NM_014354) is another VGAM1293 host target gene. HGC6.1.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGC6.1.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGC6.1.1 BINDING SITE, designated SEQ ID:15682, to the nucleotide sequence of VGAM1293 RNA, herein designated VGAM RNA, also designated SEQ ID:4004.

[45865] Another function of VGAM1293 is therefore inhibition of HGC6.1.1 (Accession NM_014354). Accordingly, utilities of

VGAM1293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGC6.1.1. Zinc Finger Protein 387 (ZNF387, Accession NM_014682) is another VGAM1293 host target gene. ZNF387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF387 BINDING SITE, designated SEQ ID:16170, to the nucleotide sequence of VGAM1293 RNA, herein designated VGAM RNA, also designated SEQ ID:4004.

[45866] Another function of VGAM1293 is therefore inhibition of Zinc Finger Protein 387 (ZNF387, Accession NM_014682). Accordingly, utilities of VGAM1293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF387. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1294 (VGAM1294) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host

target genes is known in the art.

[45867] VGAM1294 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1294 was detected is described hereinabove with reference to Figs. 1–8.

[45868] VGAM1294 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45869] VGAM1294 gene encodes a VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1294 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1294 precursor RNA is designated SEQ ID:1280, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1280 is located at position 8120 relative to the genome of Vaccinia Virus.

[45870] VGAM1294 precursor RNA folds onto itself, forming VGAM1294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45871] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1294 folded precursor RNA into VGAM1294 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1294 RNA is designated SEQ ID:4005, and is provided hereinbelow with reference to the sequence listing part.

[45872] VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1294 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45873] VGAM1294 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1294 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1294 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45874] The complementary binding of VGAM1294 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1294 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1294

host target RNA into VGAM1294 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45875] It is appreciated that VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1294 host target genes. The mRNA of each one of this plurality of VGAM1294 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1294 RNA, herein designated VGAM RNA, and which when bound by VGAM1294 RNA causes inhibition of translation of respective one or more VGAM1294 host target proteins.

[45876] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1294 gene, herein designated VGAM GENE, on one or more VGAM1294 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45877] It is yet further appreciated that a function of VGAM1294 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1294 correlate with, and may be deduced from, the identity of the host target genes which VGAM1294 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45878] Nucleotide sequences of the VGAM1294 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1294 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1294 are further

described hereinbelow with reference to Table 1.

[45879] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1294 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1294 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45880] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1294 gene, herein designated VGAM is inhibition of expression of VGAM1294 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1294 correlate with, and may be deduced from, the identity of the target genes which VGAM1294 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45881] ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM_001089) is a VGAM1294 host target gene. ABCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ABCA3 BINDING SITE, designated SEQ ID:6744, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45882] A function of VGAM1294 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM_001089), a gene which may be a transporter, may act as an efflux pump for chemotherapeutics drugs. Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA3. The function of ABCA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM336. Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812) is another VGAM1294 host target gene. BAALC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAALC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAALC BINDING SITE, designated SEQ ID:24197, to the nucleotide sequence of VGAM1294 RNA,

herein designated VGAM RNA, also designated SEQ ID:4005.

[45883] Another function of VGAM1294 is therefore inhibition of Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAALC. CERD4 (Accession NM_012074) is another VGAM1294 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14343, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45884] Another function of VGAM1294 is therefore inhibition of CERD4 (Accession NM_012074). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM_006693) is another VGAM1294

host target gene. CPSF4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CPSF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPSF4 BINDING SITE, designated SEQ ID:13512, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45885] Another function of VGAM1294 is therefore inhibition of Cleavage and Polyadenylation Specific Factor 4, 30kDa (CPSF4, Accession NM_006693), a gene which may bind DNA. Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPSF4. The function of CPSF4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM998.HYA22 (Accession NM_005808) is another VGAM1294 host target gene. HYA22 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HYA22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HYA22 BINDING SITE, designated SEQ ID:12385, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45886] Another function of VGAM1294 is therefore inhibition of HYA22 (Accession NM_005808). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYA22. KIAA1078 (Accession XM_036589) is another VGAM1294 host target gene. KIAA1078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1078 BINDING SITE, designated SEQ ID:32472, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45887] Another function of VGAM1294 is therefore inhibition of KIAA1078 (Accession XM_036589). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1078. LOC145842 (Accession XM_085254) is another VGAM1294 host target gene. LOC145842 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145842 BINDING SITE, designated SEQ ID:37998, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45888] Another function of VGAM1294 is therefore inhibition of LOC145842 (Accession XM_085254). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145842. LOC203378 (Accession XM_117541) is another VGAM1294 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43561, to the nucleotide sequence of VGAM1294 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4005.

[45889] Another function of VGAM1294 is therefore inhibition of LOC203378 (Accession XM_117541). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. LOC253975 (Accession XM_171130) is another VGAM1294 host target gene. LOC253975 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253975 BINDING SITE, designated SEQ ID:45937, to the nucleotide sequence of VGAM1294 RNA, herein designated VGAM RNA, also designated SEQ ID:4005.

[45890] Another function of VGAM1294 is therefore inhibition of LOC253975 (Accession XM_171130). Accordingly, utilities of VGAM1294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253975. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1295 (VGAM1295) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45891] VGAM1295 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1295 was detected is described hereinabove with reference to Figs. 1–8.

[45892] VGAM1295 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45893] VGAM1295 gene encodes a VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1295 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1295 precursor RNA is designated SEQ ID:1281, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1281 is located at position 10613 relative to the genome of Vaccinia Virus.

[45894] VGAM1295 precursor RNA folds onto itself, forming

VGAM1295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45895] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1295 folded precursor RNA into VGAM1295 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1295 RNA is designated SEQ ID:4006, and is provided hereinbelow with reference to the sequence listing part.

[45896] VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1295 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45897] VGAM1295 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1295 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1295 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45898] The complementary binding of VGAM1295 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1295 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1295 host target RNA into VGAM1295 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45899] It is appreciated that VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1295 host target genes. The mRNA of each one of this plurality of VGAM1295 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1295 RNA, herein designated VGAM RNA, and which when bound by VGAM1295 RNA causes inhibition of translation of respective one or more VGAM1295 host target proteins.

[45900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1295 gene, herein designated VGAM GENE, on one or more VGAM1295 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45901] It is yet further appreciated that a function of VGAM1295 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1295 correlate with, and may be deduced from, the identity of the host target genes which VGAM1295 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[45902] Nucleotide sequences of the VGAM1295 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1295 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1295 are further described hereinbelow with reference to Table 1.

[45903] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1295 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1295 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45904] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1295 gene, herein designated VGAM is inhibition of expression of VGAM1295 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1295 correlate with, and may be deduced from, the identity of the target genes which VGAM1295 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[45905] Centrosomal Protein 1 (CEP1, Accession NM_007018) is a VGAM1295 host target gene. CEP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP1 BINDING SITE, designated SEQ ID:13874, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45906] A function of VGAM1295 is therefore inhibition of Centrosomal Protein 1 (CEP1, Accession NM_007018), a gene which mediates actin cytoskeleton reorganization at the plasma membrane. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP1. The function of CEP1 has been established by previous studies.

Hemonectin is an extracellular matrix cytoadhesive protein that promotes the attachment of developing bone marrow granulocytic cells to bone marrow stroma. By immunoscreening an endothelial cell cDNA library with a polyclonal anti-rabbit hemonectin antibody and probing

an oligo(dT)–primed library, Bahou et al. (1992) obtained a cDNA encoding MSE55. Sequence analysis predicted that the 391–amino acid serum protein lacks a signal peptide but contains a series of 8 proline/alanine repeats as well as EF–hand motifs. Southern blot analysis suggested that the MSE55 gene is conserved in primates, dogs, and ducks. Northern blot analysis detected a 2.5–kb MSE55 transcript in endothelial and K562 cells; expression was not detected in monocytic, myeloid, erythroleukemic, or lymphocytic cell lines. Immunoblot analysis showed expression of a 55–kD protein in endothelial cell lines and serum. Because antibody raised against MSE55 did not recognize hemonectin and anti–hemonectin antibody did not react with the recombinant protein, Bahou et al.

(1992) concluded that hemonectin and MSE55 are distinct.

Burbelo et al. (1995) identified a 16–amino acid CDC42 (OMIM Ref. No. 116952)/RAC (OMIM Ref. No. 602048) interactive–binding (CRIB) region in a number of kinase and nonkinase proteins, including MSE55. MSE55, a nonkinase, bound more strongly to the GTP form of CDC42 than to RAC. Burbelo et al. (1999) showed that MSE55 increases membrane actin polymerization and induces the formation of long, actin–based protrusions in fibroblasts.

They concluded that MSE55 is a CDC42 effector protein that mediates actin cytoskeleton reorganization at the plasma membrane.

[45907] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45908] Burbelo, P. D.; Drechsel, D.; Hall, A. : A conserved binding motif defines numerous candidate target proteins for both Cdc42 and Rac GTPases. J. Biol. Chem. 270: 29071–29074, 1995. ; and

[45909] Burbelo, P. D.; Snow, D. M.; Bahou, W.; Spiegel, S. : MSE55, a Cdc42 effector protein, induces long cellular extensions in fibroblasts. Proc. Nat. Acad. Sci. 96: 9083–9088, 1999.

[45910] Further studies establishing the function and utilities of CEP1 are found in John Hopkins OMIM database record ID 606084, and in cited publications numbered 4425–442 and 4908 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.UDP–N–acetyl–alpha–D–galactosamine:polypeptide N–acetylgalactosaminyltransferase 7 (GalNAc–T7) (GALNT7, Accession NM_017423) is another VGAM1295 host target gene. GALNT7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by GALNT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT7 BINDING SITE, designated SEQ ID:18879, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45911] Another function of VGAM1295 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7) (GALNT7, Accession NM_017423). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT7. Gap Junction Protein, Alpha 1, 43kDa (connexin 43) (GJA1, Accession NM_000165) is another VGAM1295 host target gene. GJA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GJA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJA1 BINDING SITE, designated SEQ ID:5676, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ

ID:4006.

[45912] Another function of VGAM1295 is therefore inhibition of Gap Junction Protein, Alpha 1, 43kDa (connexin 43) (GJA1, Accession NM_000165), a gene which may act in synchronizing heart contraction and embryonic development. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJA1. The function of GJA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM341. Phosphomannomutase 2 (PMM2, Accession XM_050755) is another VGAM1295 host target gene.

PMM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMM2 BINDING SITE, designated SEQ

ID:35676, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ

ID:4006.

[45913] Another function of VGAM1295 is therefore inhibition of

Phosphomannomutase 2 (PMM2, Accession XM_050755). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMM2. RalA Binding Protein 1 (RALBP1, Accession NM_006788) is another VGAM1295 host target gene. RALBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RALBP1 BINDING SITE, designated SEQ ID:13655, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45914] Another function of VGAM1295 is therefore inhibition of RalA Binding Protein 1 (RALBP1, Accession NM_006788), a gene which plays a role in signal transduction and catalyzes the transport of glutathione conjugates and xenobiotics. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALBP1. The function of RALBP1 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM345. Ubiquilin 1 (UBQLN1, Accession NM_013438) is another VGAM1295 host target gene. UBQLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBQLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBQLN1 BINDING SITE, designated SEQ ID:15100, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45915] Another function of VGAM1295 is therefore inhibition of Ubiquilin 1 (UBQLN1, Accession NM_013438), a gene which may have a role in regulating cell cycle progression. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBQLN1. The function of UBQLN1 has been established by previous studies. By screening a human nigra cDNA library with a rat DA41 cDNA as a probe, Hanaoka et al. (2000) isolated the human DA41 homolog. Human DA41 encodes a 589-amino acid protein with a predicted molecular mass of 62.4 kD. The protein shows 86% amino acid sequence identity with the rat pro-

tein, indicating the evolutionarily conserved structure and function of DA41. DA41 was expressed ubiquitously in adult human tissues, with relatively higher levels in pituitary gland, adrenal gland, kidney, thymus, and placenta. By performing independent yeast 2-hybrid screens, Kleijnen et al. (2000) isolated cDNAs encoding PLIC1 and PLIC2 (UBQLN2; 300264), homologs of the mouse Plics (proteins linking integrin-associated protein (IAP; 601028) and cytoskeleton) and the yeast Dsk2 protein. PLIC1, also called UBQLN1, shares 72% amino acid identity with PLIC2. Two motifs are conserved in the mammalian PLICs and yeast Dsk2, an N-terminal ubiquitin (OMIM Ref. No. 191320)-like (UBL) domain and a C-terminal ubiquitin-associated (UBA) domain. Unlike ubiquitin, the UBL domain of the PLICs does not have a diglycine motif in its C terminus; the diglycine motif serves as a target site for cellular hydrolases that release ubiquitin from precursor fusion proteins. The absence of a GG sequence suggests that the UBL domain in the PLICs is an integral part of the open reading frame. The UBA domain is a loosely defined sequence motif present in multiple enzyme classes of the ubiquitination machinery. The most notable difference between the mammalian PLICs is the presence of a colla-

gen-like motif in PLIC2 that is absent in PLIC1 and yeast Dsk2. This domain is most homologous to the collagen-like oncoprotein of herpesvirus Saimiri, STP-C488, which is implicated in intracellular signaling via the RAS-RAF pathway (see OMIM Ref. No. 190020). The collagen-like domain of PLIC2 contains 8 PXGP motifs that are susceptible to cleavage by collagenase in vitro. Kleijnen et al (2000) showed that the human PLICs physically associate with both proteasomes and ubiquitin ligases in large complexes. Overexpression of PLICs interfered with the in vivo degradation of 2 unrelated ubiquitin-dependent proteasome substrates, p53 (OMIM Ref. No. 191170) and I-kappa-B-alpha (NFKBIA; 164008), but not a ubiquitin-independent substrate. These findings raised the possibility that the PLICs, and possibly related ubiquitin-like family members, may functionally link the ubiquitination machinery to the proteasome to affect in vivo protein degradation.

[45916] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45917] Hanaoka, E.; Ozaki, T.; Ohira, M.; Nakamura, Y.; Suzuki, M.; Takahashi, E.; Moriya, H.; Nakagawara, A.; Sakiyama,

S. : Molecular cloning and expression analysis of the human DA41 gene and its mapping to chromosome

9q21.2–q21.3. J. Hum. Genet. 45: 188–191, 2000. ; and

[45918] Kleijnen, M. F.; Shih, A. H.; Zhou, P.; Kumar, S.; Soccio, R. E.; Kedersha, N. L.; Gill, G.; Howley, P. M. : The hPLIC proteins may provide a link between the ubiquitination machinery.

[45919] Further studies establishing the function and utilities of UBQLN1 are found in John Hopkins OMIM database record ID 605046, and in cited publications numbered 659 and 10635 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquilin 2 (UBQLN2, Accession NM_013444) is another VGAM1295 host target gene. UBQLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBQLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBQLN2 BINDING SITE, designated SEQ ID:15111, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45920] Another function of VGAM1295 is therefore inhibition of

Ubiquilin 2 (UBQLN2, Accession NM_013444), a gene which is involved in spindle pole body duplication with rad23. Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBQLN2. The function of UBQLN2 has been established by previous studies. By performing independent yeast 2-hybrid screens, Kleijnen et al. (2000) isolated cDNAs encoding PLIC1 (UBQLN1; 605046) and PLIC2, homologs of the mouse Plics (proteins linking integrin-associated protein (IAP; 601028) and cytoskeleton) and the yeast Dsk2 protein. The predicted 624-amino acid PLIC2 protein, also called UBQLN2, shares 72% amino acid identity with PLIC1. Two motifs are conserved in the mammalian PLICs and yeast Dsk2, an N-terminal ubiquitin (OMIM Ref. No. 191320)-like (UBL) domain and a C-terminal ubiquitin-associated (UBA) domain. Unlike ubiquitin, the UBL domain of the PLICs does not have a diglycine motif in its C terminus; the diglycine motif serves as a target site for cellular hydrolases that release ubiquitin from precursor fusion proteins. The absence of a GG sequence suggests that the UBL domain in the PLICs is an integral part of the open reading frame. The UBA domain is a loosely defined sequence motif

present in multiple enzyme classes of the ubiquitination machinery. The most notable difference between the mammalian PLICs is the presence of a collagen-like motif in PLIC2 that is absent in PLIC1 and yeast Dsk2. This domain is most homologous to the collagen-like oncoprotein of herpesvirus Saimiri, STP-C488, which is implicated in intracellular signaling via the RAS-RAF pathway (see OMIM Ref. No. 190020). The collagen-like domain of PLIC2 contains 8 PXGP motifs that are susceptible to cleavage by collagenase in vitro. Kleijnen et al (2000) showed that the human PLICs physically associate with both proteasomes and ubiquitin ligases in large complexes. Overexpression of PLICs interfered with the in vivo degradation of 2 unrelated ubiquitin-dependent proteasome substrates, p53 (OMIM Ref. No. 191170) and I-kappa-B-alpha (NFKBIA; 164008), but not a ubiquitin-independent substrate. These findings raised the possibility that the PLICs, and possibly related ubiquitin-like family members, may functionally link the ubiquitination machinery to the proteasome to affect in vivo protein degradation. By screening a human lung 2-hybrid cDNA library using a pGBT9-STCH (OMIM Ref. No. 601100) plasmid as bait, Kaye et al. (2000) isolated a cDNA encoding UBQLN2,

which they termed CHAP1/DSK2. Mutation analysis determined that the C-terminal Sti1-like repeat sequence, but neither the N-terminal UBL domain nor the C-terminal UBA domain, is required for binding of UBQLN2 to the ATPase domain of STCH.

[45921] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45922] Kaye, F. J.; Shows, T. B. : Assignment of ubiquilin 2 (UBQLN2) to human chromosome xp11.23-p11.1 by GeneBridge radiation hybrids. Cytogenet. Cell Genet. 89: 116-117, 2000. ; and

[45923] Kleijnen, M. F.; Shih, A. H.; Zhou, P.; Kumar, S.; Soccio, R. E.; Kedersha, N. L.; Gill, G.; Howley, P. M. : The hPLIC proteins may provide a link between the ubiquitination machinery.

[45924] Further studies establishing the function and utilities of UBQLN2 are found in John Hopkins OMIM database record ID 300264, and in cited publications numbered 10633-10635 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916) is another VGAM1295

host target gene. AP1S2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1S2 BINDING SITE, designated SEQ ID:10001, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45925] Another function of VGAM1295 is therefore inhibition of Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1S2. Claudin 1 (CLDN1, Accession NM_021101) is another VGAM1295 host target gene. CLDN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN1 BINDING SITE, designated SEQ ID:22080, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA,

also designated SEQ ID:4006.

[45926] Another function of VGAM1295 is therefore inhibition of Claudin 1 (CLDN1, Accession NM_021101). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN1. dA141H5.1 (Accession NM_145234) is another VGAM1295 host target gene. dA141H5.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by dA141H5.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of dA141H5.1 BINDING SITE, designated SEQ ID:29747, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45927] Another function of VGAM1295 is therefore inhibition of dA141H5.1 (Accession NM_145234). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with dA141H5.1. FHX (Accession NM_018416) is another VGAM1295 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHX, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20460, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45928] Another function of VGAM1295 is therefore inhibition of FHX (Accession NM_018416). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHX. FLJ20254 (Accession NM_017727) is another VGAM1295 host target gene. FLJ20254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20254 BINDING SITE, designated SEQ ID:19315, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45929] Another function of VGAM1295 is therefore inhibition of FLJ20254 (Accession NM_017727). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20254. FLJ22690 (Accession NM_024711) is another VGAM1295 host target gene. FLJ22690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22690 BINDING SITE, designated SEQ ID:24036, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45930] Another function of VGAM1295 is therefore inhibition of FLJ22690 (Accession NM_024711). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22690. Ganglioside-induced Differentiation-associated Protein 1-like 1 (GDAP1L1, Accession NM_024034) is another VGAM1295 host target gene. GDAP1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GDAP1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

GDAP1L1 BINDING SITE, designated SEQ ID:23465, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45931] Another function of VGAM1295 is therefore inhibition of Ganglioside-induced Differentiation-associated Protein 1-like 1 (GDAP1L1, Accession NM_024034). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GDAP1L1. Glia Maturation Factor, Beta (GMFB, Accession NM_004124) is another VGAM1295 host target gene. GMFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GMFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMFB BINDING SITE, designated SEQ ID:10330, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45932] Another function of VGAM1295 is therefore inhibition of Glia Maturation Factor, Beta (GMFB, Accession NM_004124). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMFB. KIAA0254 (Accession

NM_014758) is another VGAM1295 host target gene. KIAA0254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0254 BINDING SITE, designated SEQ ID:16502, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45933] Another function of VGAM1295 is therefore inhibition of KIAA0254 (Accession NM_014758). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0254. KIAA1524 (Accession XM_056015) is another VGAM1295 host target gene. KIAA1524 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1524 BINDING SITE, designated SEQ ID:36359, to the nucleotide sequence of VGAM1295 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4006.

[45934] Another function of VGAM1295 is therefore inhibition of KIAA1524 (Accession XM_056015). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1524. MGC13007 (Accession NM_032320) is another VGAM1295 host target gene. MGC13007 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC13007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13007 BINDING SITE, designated SEQ ID:26119, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45935] Another function of VGAM1295 is therefore inhibition of MGC13007 (Accession NM_032320). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13007. Phytoceramidase, Alkaline (PHCA, Accession NM_018367) is another VGAM1295 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PHCA,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20378, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45936] Another function of VGAM1295 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM_018367). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. PRO1580 (Accession NM_018502) is another VGAM1295 host target gene. PRO1580 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1580 BINDING SITE, designated SEQ ID:20565, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45937] Another function of VGAM1295 is therefore inhibition of PRO1580 (Accession NM_018502). Accordingly, utilities of

VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1580. LOC126661 (Accession XM_059061) is another VGAM1295 host target gene. LOC126661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126661 BINDING SITE, designated SEQ ID:36855, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45938] Another function of VGAM1295 is therefore inhibition of LOC126661 (Accession XM_059061). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126661. LOC158364 (Accession XM_088546) is another VGAM1295 host target gene. LOC158364 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC158364 BINDING SITE, designated SEQ ID:39813, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45939] Another function of VGAM1295 is therefore inhibition of LOC158364 (Accession XM_088546). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158364. LOC197319 (Accession XM_113862) is another VGAM1295 host target gene. LOC197319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197319 BINDING SITE, designated SEQ ID:42475, to the nucleotide sequence of VGAM1295 RNA, herein designated VGAM RNA, also designated SEQ ID:4006.

[45940] Another function of VGAM1295 is therefore inhibition of LOC197319 (Accession XM_113862). Accordingly, utilities of VGAM1295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1296 (VGAM1296) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45941] VGAM1296 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1296 was detected is described hereinabove with reference to Figs. 1–8.

[45942] VGAM1296 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Vaccinia Virus. VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45943] VGAM1296 gene encodes a VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1296 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1296 precursor RNA is designated SEQ ID:1282, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1282 is located at position 11590 relative to the

genome of Vaccinia Virus.

[45944] VGAM1296 precursor RNA folds onto itself, forming VGAM1296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45945] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1296 folded precursor RNA into VGAM1296 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1296 RNA is designated SEQ ID:4007, and is provided hereinbelow with reference to the sequence listing part.

[45946] VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1296 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45947] VGAM1296 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1296 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1296 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[45948] The complementary binding of VGAM1296 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1296 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1296 host target RNA into VGAM1296 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45949] It is appreciated that VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1296 host target genes. The mRNA of each one of this plurality of VGAM1296 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1296 RNA, herein designated VGAM RNA, and which when bound by VGAM1296 RNA causes inhibition of translation of respective one or more VGAM1296 host target proteins.

[45950] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1296 gene, herein designated VGAM GENE, on one or more VGAM1296 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45951] It is yet further appreciated that a function of VGAM1296 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGAM1296 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1296 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45952] Nucleotide sequences of the VGAM1296 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1296 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1296 are further described hereinbelow with reference to Table 1.

[45953] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1296 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1296 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45954] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1296 gene, herein designated VGAM is inhibition of expression of VGAM1296 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1296 correlate with, and may be deduced

from, the identity of the target genes which VGAM1296 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45955] B-cell Translocation Gene 1, Anti-proliferative (BTG1, Accession NM_001731) is a VGAM1296 host target gene. BTG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG1 BINDING SITE, designated SEQ ID:7465, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45956] A function of VGAM1296 is therefore inhibition of B-cell Translocation Gene 1, Anti-proliferative (BTG1, Accession NM_001731), a gene which is a member of a new family of antiproliferative proteins. Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG1. The function of BTG1 has been established by previous studies. Rimokh et al. (1991) cloned the breakpoint of a t(8;12) chromosomal translocation in a case of B-cell chronic lymphocytic leukemia and isolated a coding se-

quence mapping on 12q22. This sequence detected a 1.8-kb transcript in virtually all tissues tested except in the brain and muscle where the signal was barely detectable. The putative gene corresponding to this sequence, termed BTG1 for B-cell translocation gene 1, was shown to be highly conserved in evolution; a similar 1.8-kb transcript could be detected in murine and chicken tissue by using a human BTG1 DNA probe. Rouault et al. (1992) established the genomic organization of the gene. The full-length cDNA isolated from a lymphoblastoid cell line contained an open reading frame of 171 amino acids. BTG1 expression was maximal in the G0/G1 phases of the cell cycle and downregulated when cells progressed throughout G1. Furthermore, transfection experiments using NIH 3T3 cells indicated that BTG1 negatively regulates cell proliferation. Rouault et al. (1992) postulated that BTG1 is a member of a new family of antiproliferative genes

[45957] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[45958] Rouault, J.-P.; Rimokh, R.; Tessa, C.; Paranhos, G.; Ffrench, M.; Duret, L.; Garoccio, M.; Germain, D.; Samarut,

J.; Magaud, J.-P. : BTG1, a member of a new family of anti-proliferative genes. EMBO J. 11: 1663–1670, 1992. ; and

[45959] Rimokh, R.; Rouault, J. P.; Wahbi, K.; Gadoux, M.; Lafage, M.; Archimbaud, E.; Charrin, C.; Gentilhomme, O.; Germain, D.; Samarut, J.; Magaud, J. P. : A chromosome 12 coding region is ju.

[45960] Further studies establishing the function and utilities of BTG1 are found in John Hopkins OMIM database record ID 109580, and in cited publications numbered 138 and 1445 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BH-protocadherin (brain-heart) (PCDH7, Accession NM_002589) is another VGAM1296 host target gene. PCDH7 BINDING SITE1 through PCDH7 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH7 BINDING SITE1 through PCDH7 BINDING SITE3, designated SEQ ID:8452, SEQ ID:26217 and SEQ ID:26220 respectively, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45961] Another function of VGAM1296 is therefore inhibition of BH-protocadherin (brain-heart) (PCDH7, Accession NM_002589). Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH7. KIAA1950 (Accession XM_166532) is another VGAM1296 host target gene. KIAA1950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1950 BINDING SITE, designated SEQ ID:44484, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45962] Another function of VGAM1296 is therefore inhibition of KIAA1950 (Accession XM_166532). Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1950. MAC30 (Accession XM_031536) is another VGAM1296 host target gene. MAC30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAC30, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAC30 BINDING SITE, designated SEQ ID:31407, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45963] Another function of VGAM1296 is therefore inhibition of MAC30 (Accession XM_031536). Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAC30. LOC147219 (Accession XM_097214) is another VGAM1296 host target gene. LOC147219 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147219 BINDING SITE, designated SEQ ID:40823, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45964] Another function of VGAM1296 is therefore inhibition of LOC147219 (Accession XM_097214). Accordingly, utilities of VGAM1296 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC147219. LOC150174 (Accession XM_086802) is another VGAM1296 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150174 BINDING SITE, designated SEQ ID:38867, to the nucleotide sequence of VGAM1296 RNA, herein designated VGAM RNA, also designated SEQ ID:4007.

[45965] Another function of VGAM1296 is therefore inhibition of LOC150174 (Accession XM_086802). Accordingly, utilities of VGAM1296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1297 (VGAM1297) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45966] VGAM1297 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1297 was detected is described hereinabove with reference to Figs. 1–8.

[45967] VGAM1297 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45968] VGAM1297 gene encodes a VGAM1297 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1297 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1297 precursor RNA is designated SEQ ID:1283, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1283 is located at position 75507 relative to the genome of Yaba-like Disease Virus.

[45969] VGAM1297 precursor RNA folds onto itself, forming VGAM1297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[45970] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1297 folded precursor RNA into VGAM1297 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1297 RNA is designated SEQ ID:4008, and is provided hereinbelow with reference to the sequence listing part.

[45971] VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1297 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45972] VGAM1297 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1297 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1297 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45973] The complementary binding of VGAM1297 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1297 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1297 host target RNA into VGAM1297 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45974] It is appreciated that VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1297 host target genes. The mRNA of each one of this plurality of VGAM1297 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1297 RNA, herein designated VGAM RNA, and which when bound by VGAM1297 RNA causes inhibition of translation of respective one or more VGAM1297 host target proteins.

[45975] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1297 gene, herein designated VGAM GENE, on one or more VGAM1297 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[45976] It is yet further appreciated that a function of VGAM1297 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1297 correlate with, and may be deduced from, the identity of the host target genes which VGAM1297 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[45977] Nucleotide sequences of the VGAM1297 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1297 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1297 are further described hereinbelow with reference to Table 1.

[45978] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1297 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1297 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[45979] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1297 gene, herein designated VGAM is inhibition of expression of VGAM1297 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1297 correlate with, and may be deduced from, the identity of the target genes which VGAM1297 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[45980] Reserved (C8orf6, Accession XM_114624) is a VGAM1297 host target gene. C8orf6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA

encoded by C8orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf6 BINDING SITE, designated SEQ ID:43004, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45981] A function of VGAM1297 is therefore inhibition of Reserved (C8orf6, Accession XM_114624). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf6. FLJ10193 (Accession NM_018019) is another VGAM1297 host target gene. FLJ10193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10193 BINDING SITE, designated SEQ ID:19760, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45982] Another function of VGAM1297 is therefore inhibition of FLJ10193 (Accession NM_018019). Accordingly, utilities of

VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10193. FLJ30532 (Accession NM_144724) is another VGAM1297 host target gene. FLJ30532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30532 BINDING SITE, designated SEQ ID:29548, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45983] Another function of VGAM1297 is therefore inhibition of FLJ30532 (Accession NM_144724). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30532. KIAA0537 (Accession NM_014840) is another VGAM1297 host target gene. KIAA0537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0537 BINDING SITE, designated SEQ ID:16863, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45984] Another function of VGAM1297 is therefore inhibition of KIAA0537 (Accession NM_014840). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0537. KIAA0596 (Accession XM_031706) is another VGAM1297 host target gene. KIAA0596 BINDING SITE1 and KIAA0596 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0596, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0596 BINDING SITE1 and KIAA0596 BINDING SITE2, designated SEQ ID:31466 and SEQ ID:31464 respectively, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45985] Another function of VGAM1297 is therefore inhibition of KIAA0596 (Accession XM_031706). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0596. KIAA1766 (Accession XM_049218) is another VGAM1297 host target gene. KIAA1766 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1766 BINDING SITE, designated SEQ ID:35353, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45986] Another function of VGAM1297 is therefore inhibition of KIAA1766 (Accession XM_049218). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1766. LAGY (Accession NM_139212) is another VGAM1297 host target gene. LAGY BINDING SITE1 through LAGY BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LAGY, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAGY BINDING SITE1 through LAGY BINDING SITE3, designated SEQ ID:29234, SEQ ID:26246 and SEQ

ID:29232 respectively, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45987] Another function of VGAM1297 is therefore inhibition of LAGY (Accession NM_139212). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAGY. LOC124152 (Accession XM_058777) is another VGAM1297 host target gene. LOC124152 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124152, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124152 BINDING SITE, designated SEQ ID:36737, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45988] Another function of VGAM1297 is therefore inhibition of LOC124152 (Accession XM_058777). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124152. LOC158835 (Accession XM_088683) is another VGAM1297 host target gene. LOC158835 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158835, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158835 BINDING SITE, designated SEQ ID:39895, to the nucleotide sequence of VGAM1297 RNA, herein designated VGAM RNA, also designated SEQ ID:4008.

[45989] Another function of VGAM1297 is therefore inhibition of LOC158835 (Accession XM_088683). Accordingly, utilities of VGAM1297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158835. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1298 (VGAM1298) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[45990] VGAM1298 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1298 was detected is described hereinabove with reference to Figs. 1-8.

[45991] VGAM1298 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[45992] VGAM1298 gene encodes a VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1298 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1298 precursor RNA is designated SEQ ID:1284, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1284 is located at position 77434 relative to the genome of Yaba-like Disease Virus.

[45993] VGAM1298 precursor RNA folds onto itself, forming VGAM1298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[45994] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1298 folded precursor RNA into VGAM1298 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1298 RNA is designated SEQ ID:4009, and is provided hereinbelow with reference to the sequence listing part.

[45995] VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1298 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[45996] VGAM1298 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1298 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1298 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1298 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[45997] The complementary binding of VGAM1298 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1298 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1298 host target RNA into VGAM1298 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[45998] It is appreciated that VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1298 host target genes. The mRNA of each one of this plurality of VGAM1298 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1298 RNA, herein designated VGAM RNA, and which when bound by VGAM1298 RNA causes inhibition of translation of respective one or more VGAM1298 host target proteins.

[45999] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1298 gene, herein designated VGAM GENE, on one or more VGAM1298 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46000] It is yet further appreciated that a function of VGAM1298 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1298 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1298 correlate with, and may be deduced from, the identity of the host target genes which VGAM1298 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46001] Nucleotide sequences of the VGAM1298 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1298 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1298 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1298 are further described hereinbelow with reference to Table 1.

[46002] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1298 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1298 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46003] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1298 gene, herein designated VGAM is inhibition of expression of VGAM1298 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1298 correlate with, and may be deduced from, the identity of the target genes which VGAM1298 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46004] LOC158014 (Accession XM_088442) is a VGAM1298 host target gene. LOC158014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC158014 BINDING SITE, designated SEQ ID:39689, to the nucleotide sequence of VGAM1298 RNA, herein designated VGAM RNA, also designated SEQ ID:4009.

[46005] A function of VGAM1298 is therefore inhibition of LOC158014 (Accession XM_088442). Accordingly, utilities of VGAM1298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158014. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1299 (VGAM1299) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46006] VGAM1299 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1299 was detected is described hereinabove with reference to Figs. 1–8.

[46007] VGAM1299 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[46008] VGAM1299 gene encodes a VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1299 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1299 precursor RNA is designated SEQ ID:1285, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1285 is located at position 80251 relative to the genome of Yaba-like Disease Virus.

[46009] VGAM1299 precursor RNA folds onto itself, forming VGAM1299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46010] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1299 folded precursor RNA into VGAM1299 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1299 RNA is designated SEQ ID:4010, and is provided hereinbelow with reference to the sequence listing part.

[46011] VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1299 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46012] VGAM1299 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1299 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1299 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46013] The complementary binding of VGAM1299 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1299 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1299 host target RNA into VGAM1299 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46014] It is appreciated that VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1299 host target genes. The mRNA of each one of this plurality of VGAM1299 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1299 RNA, herein designated VGAM RNA, and which when bound by VGAM1299 RNA causes inhibition of translation of respective one or more VGAM1299 host target proteins.

[46015] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1299 gene, herein designated VGAM GENE, on one or more VGAM1299 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46016] It is yet further appreciated that a function of VGAM1299 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1299 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1299 correlate with, and may be deduced from, the identity of the host target genes which VGAM1299 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46017] Nucleotide sequences of the VGAM1299 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1299 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1299 are further described hereinbelow with reference to Table 1.

[46018] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1299 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1299 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46019] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1299 gene, herein designated VGAM is inhibition of expression of VGAM1299 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1299 correlate with, and may be deduced from, the identity of the target genes which VGAM1299 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46020] POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237) is a VGAM1299 host target gene. POU4F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU4F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU4F1 BINDING SITE, designated SEQ ID:12898, to the nucleotide sequence of VGAM1299 RNA, herein designated VGAM RNA, also designated SEQ

ID:4010.

[46021] A function of VGAM1299 is therefore inhibition of POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237), a gene which plays a role in the regulation of specific gene expression within a subset of neuronal lineages. Accordingly, utilities of VGAM1299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU4F1. The function of POU4F1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1026. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1300 (VGAM1300) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46022] VGAM1300 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1300 was detected is described hereinabove with reference to Figs. 1-8.

[46023] VGAM1300 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Yaba-like Disease Virus. VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46024] VGAM1300 gene encodes a VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1300 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1300 precursor RNA is designated SEQ ID:1286, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1286 is located at position 78499 relative to the genome of Yaba-like Disease Virus.

[46025] VGAM1300 precursor RNA folds onto itself, forming VGAM1300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46026] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1300 folded precursor RNA into VGAM1300 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1300 RNA is designated SEQ ID:4011, and is provided hereinbelow with reference to the sequence listing part.

[46027] VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1300 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46028] VGAM1300 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1300 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1300 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46029] The complementary binding of VGAM1300 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1300 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1300

host target RNA into VGAM1300 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46030] It is appreciated that VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1300 host target genes. The mRNA of each one of this plurality of VGAM1300 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1300 RNA, herein designated VGAM RNA, and which when bound by VGAM1300 RNA causes inhibition of translation of respective one or more VGAM1300 host target proteins.

[46031] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1300 gene, herein designated VGAM GENE, on one or more VGAM1300 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46032] It is yet further appreciated that a function of VGAM1300 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1300 correlate with, and may be deduced from, the identity of the host target genes which VGAM1300 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46033] Nucleotide sequences of the VGAM1300 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1300 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1300 are further

described hereinbelow with reference to Table 1.

[46034] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1300 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1300 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46035] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1300 gene, herein designated VGAM is inhibition of expression of VGAM1300 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1300 correlate with, and may be deduced from, the identity of the target genes which VGAM1300 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46036] Mab-21-like 1 (C. elegans) (MAB21L1, Accession NM_005584) is a VGAM1300 host target gene. MAB21L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAB21L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of MAB21L1 BINDING SITE, designated SEQ ID:12110, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46037] A function of VGAM1300 is therefore inhibition of Mab-21-like 1 (*C. elegans*) (MAB21L1, Accession NM_005584), a gene which may control cerebellum and eye development; very strongly similar to murine Mm.10798. Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L1. The function of MAB21L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM39. Spastic Paraplegia 3A (autosomal dominant) (SPG3A, Accession NM_015915) is another VGAM1300 host target gene. SPG3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPG3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPG3A BINDING SITE, designated SEQ ID:18046, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA,

also designated SEQ ID:4011.

[46038] Another function of VGAM1300 is therefore inhibition of Spastic Paraplegia 3A (autosomal dominant) (SPG3A, Accession NM_015915). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPG3A. C6orf5 (Accession NM_015524) is another VGAM1300 host target gene. C6orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf5 BINDING SITE, designated SEQ ID:17783, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46039] Another function of VGAM1300 is therefore inhibition of C6orf5 (Accession NM_015524). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf5. DKFZP586M0622 (Accession NM_015583) is another VGAM1300 host target gene. DKFZP586M0622 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by DKFZP586M0622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586M0622 BINDING SITE, designated SEQ ID:17849, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46040] Another function of VGAM1300 is therefore inhibition of DKFZP586M0622 (Accession NM_015583). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586M0622. FLJ14281 (Accession NM_024920) is another VGAM1300 host target gene. FLJ14281 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14281 BINDING SITE, designated SEQ ID:24450, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46041] Another function of VGAM1300 is therefore inhibition of

FLJ14281 (Accession NM_024920). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14281. KIAA1789 (Accession XM_040486) is another VGAM1300 host target gene. KIAA1789 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1789 BINDING SITE, designated SEQ ID:33315, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46042] Another function of VGAM1300 is therefore inhibition of KIAA1789 (Accession XM_040486). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1789. Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM_020841) is another VGAM1300 host target gene. OSBPL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL8 BINDING SITE, designated SEQ ID:21902, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46043] Another function of VGAM1300 is therefore inhibition of Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM_020841). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL8. Regulator of G-protein Signalling 13 (RGS13, Accession NM_144766) is another VGAM1300 host target gene. RGS13 BINDING SITE1 and RGS13 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RGS13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS13 BINDING SITE1 and RGS13 BINDING SITE2, designated SEQ ID:29557 and SEQ ID:8831 respectively, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46044] Another function of VGAM1300 is therefore inhibition of

Regulator of G-protein Signalling 13 (RGS13, Accession NM_144766). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS13. LOC51134 (Accession NM_016122) is another VGAM1300 host target gene. LOC51134 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51134 BINDING SITE, designated SEQ ID:18208, to the nucleotide sequence of VGAM1300 RNA, herein designated VGAM RNA, also designated SEQ ID:4011.

[46045] Another function of VGAM1300 is therefore inhibition of LOC51134 (Accession NM_016122). Accordingly, utilities of VGAM1300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51134. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1301 (VGAM1301) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[46046] VGAM1301 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1301 was detected is described hereinabove with reference to Figs. 1-8.

[46047] VGAM1301 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Yaba-like Disease Virus. VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46048] VGAM1301 gene encodes a VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1301 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1301 precursor RNA is designated SEQ ID:1287, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1287 is located at position 78643 relative to the genome of Yaba-like Disease Virus.

[46049] VGAM1301 precursor RNA folds onto itself, forming VGAM1301 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46050] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1301 folded precursor RNA into VGAM1301 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM1301 RNA is designated SEQ ID:4012, and is provided hereinbelow with reference to the sequence listing part.

[46051] VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1301 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46052] VGAM1301 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1301 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1301 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46053] The complementary binding of VGAM1301 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1301 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1301 host target RNA into VGAM1301 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46054] It is appreciated that VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1301 host target genes. The mRNA of each one of this plurality of VGAM1301 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1301 RNA, herein designated VGAM RNA, and which when bound by VGAM1301 RNA causes inhibition of translation of respective one or more VGAM1301 host target proteins.

[46055] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1301 gene, herein designated VGAM GENE, on one or more VGAM1301 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46056] It is yet further appreciated that a function of VGAM1301 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1301 include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGAM1301 correlate with, and may be deduced from, the identity of the host target genes which VGAM1301 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[46057] Nucleotide sequences of the VGAM1301 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1301 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1301 are further described hereinbelow with reference to Table 1.

[46058] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1301 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1301 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46059] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1301 gene, herein designated VGAM is inhibition of expression of VGAM1301 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1301 correlate with, and may be deduced from, the identity of the target genes which VGAM1301 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46060] STAF65(gamma) (Accession NM_014860) is a VGAM1301 host target gene. STAF65(gamma) BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAF65(gamma), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAF65(gamma) BINDING SITE, designated SEQ ID:16925, to the nucleotide sequence of VGAM1301 RNA, herein designated VGAM RNA, also designated SEQ ID:4012.

[46061] A function of VGAM1301 is therefore inhibition of STAF65(gamma) (Accession NM_014860). Accordingly, utilities of VGAM1301 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAF65(gamma). Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1302 (VGAM1302) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46062] VGAM1302 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1302 was detected is described hereinabove with reference to Figs. 1–8.

[46063] VGAM1302 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46064] VGAM1302 gene encodes a VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1302 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1302 precursor RNA is designated SEQ ID:1288, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1288 is located at position 180181 relative to the genome of Human Herpesvirus 5.

[46065] VGAM1302 precursor RNA folds onto itself, forming VGAM1302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46066] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1302 folded precursor RNA into VGAM1302 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1302 RNA is designated SEQ ID:4013, and is provided hereinbelow with reference to the sequence listing part.

[46067] VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1302 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46068] VGAM1302 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1302 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1302 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[46069] The complementary binding of VGAM1302 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1302 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1302 host target RNA into VGAM1302 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46070] It is appreciated that VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1302 host target genes. The mRNA of each one of this plurality of VGAM1302 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1302 RNA, herein designated VGAM RNA, and which when bound by VGAM1302 RNA causes inhibition of translation of respective one or more VGAM1302 host target proteins.

[46071] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1302 gene, herein designated VGAM GENE, on one or more VGAM1302 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46072] It is yet further appreciated that a function of VGAM1302 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1302 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1302 correlate with, and may be deduced from, the identity of the host target genes which VGAM1302 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46073] Nucleotide sequences of the VGAM1302 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1302 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1302 are further described hereinbelow with reference to Table 1.

[46074] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1302 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1302 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46075] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1302 gene, herein designated VGAM is inhibition of expression of VGAM1302 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1302 correlate with, and may be deduced from, the identity of the target genes which VGAM1302 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46076] LOC254528 (Accession XM_170797) is a VGAM1302 host target gene. LOC254528 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254528, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254528 BINDING SITE, designated SEQ ID:45566, to the nucleotide sequence of VGAM1302 RNA, herein designated VGAM RNA, also designated SEQ ID:4013.

[46077] A function of VGAM1302 is therefore inhibition of LOC254528 (Accession XM_170797). Accordingly, utilities of VGAM1302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254528. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1303 (VGAM1303) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46078] VGAM1303 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1303 was detected is described hereinabove with reference to Figs. 1-8.

[46079] VGAM1303 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5.

VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46080] VGAM1303 gene encodes a VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1303 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1303 precursor RNA is designated SEQ ID:1289, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1289 is located at position 177616 relative to the genome of Human Herpesvirus 5.

[46081] VGAM1303 precursor RNA folds onto itself, forming VGAM1303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46082] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1303 folded precursor RNA into VGAM1303 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1303 RNA is designated SEQ ID:4014, and is provided hereinbelow with reference to the sequence listing part.

[46083] VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1303 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46084] VGAM1303 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1303 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1303 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46085] The complementary binding of VGAM1303 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1303 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1303 host target RNA into VGAM1303 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46086] It is appreciated that VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1303 host target genes. The mRNA of each one of this plurality of VGAM1303 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1303 RNA, herein designated VGAM RNA, and which when bound by VGAM1303 RNA causes inhibition of translation of respective one or more VGAM1303 host target proteins.

[46087] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1303 gene, herein designated VGAM GENE, on one or more VGAM1303 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46088] It is yet further appreciated that a function of VGAM1303 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1303 correlate with, and may be deduced from, the identity of the host target genes which VGAM1303 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46089] Nucleotide sequences of the VGAM1303 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1303 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1303 are further described hereinbelow with reference to Table 1.

[46090] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1303 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1303 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46091] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1303 gene, herein designated VGAM is inhibition of expression of VGAM1303 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1303 correlate with, and may be deduced from, the identity of the target genes which VGAM1303 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46092] Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is a VGAM1303 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10696, to the nu-

cleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46093] A function of VGAM1303 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. E2F Transcription Factor 3 (E2F3, Accession NM_001949) is another VGAM1303 host target gene. E2F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by E2F3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2F3 BINDING SITE, designated SEQ ID:7667, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46094] Another function of VGAM1303 is therefore inhibition of E2F Transcription Factor 3 (E2F3, Accession NM_001949),

a gene which binds dna and controls cell-cycle progression from g1 to s phase. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F3. The function of E2F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069) is another VGAM1303 host target gene. GNAI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI1 BINDING SITE, designated SEQ ID:7839, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46095] Another function of VGAM1303 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069), a gene which is involved as modulators or

transducers in various transmembrane signaling systems. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI1. The function of GNAI1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Heparanase (HPSE, Accession NM_006665) is another VGAM1303 host target gene. HPSE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPSE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPSE BINDING SITE, designated SEQ ID:13476, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46096] Another function of VGAM1303 is therefore inhibition of Heparanase (HPSE, Accession NM_006665), a gene which is an endoglycosidase that cleaves heparan sulfate. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPSE. The function of HPSE and its associ-

ation with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM374. Interleukin 1 Receptor, Type I (IL1R1, Accession NM_000877) is another VGAM1303 host target gene. IL1R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1R1 BINDING SITE, designated SEQ ID:6565, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46097] Another function of VGAM1303 is therefore inhibition of Interleukin 1 Receptor, Type I (IL1R1, Accession NM_000877), a gene which is a receptor for interleukin-1 alpha (il-1a), beta (il-1b), and interleukin-1 receptor antagonist protein (il-1ra). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1R1. The function of IL1R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM704.MAD, Mothers Against Decapentaplegic Homolog 4 (Drosophila) (MADH4, Accession NM_005359) is another VGAM1303 host target gene. MADH4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MADH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH4 BINDING SITE, designated SEQ ID:11832, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46098] Another function of VGAM1303 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog 4 (Drosophila) (MADH4, Accession NM_005359), a gene which common mediator of signal transduction by $\text{tgf-}\beta$ (transforming growth factor) superfamily; *smad4* is the common *smad* (co-*smad*). promotes binding of the *smad2/sm**ad4*/*fast-1* complex to dna and provides an activation function required for *smad1* or *smad2* to stimulate transcription. may act as a tumor suppressor. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH4. The function of MADH4 and its associ-

ation with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. Regulator of G-protein Signalling 3 (RGS3, Accession NM_021106) is another VGAM1303 host target gene. RGS3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RGS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS3 BINDING SITE, designated SEQ ID:22089, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46099] Another function of VGAM1303 is therefore inhibition of Regulator of G-protein Signalling 3 (RGS3, Accession NM_021106), a gene which negatively regulates G protein-coupled receptor signalling. Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS3. The function of RGS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404.DKFZp434G179 (Accession XM_087065) is

another VGAM1303 host target gene. DKFZp434G179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434G179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434G179 BINDING SITE, designated SEQ ID:39040, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46100] Another function of VGAM1303 is therefore inhibition of DKFZp434G179 (Accession XM_087065). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434G179. DKFZP434J037 (Accession NM_030952) is another VGAM1303 host target gene. DKFZP434J037 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434J037, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J037 BINDING SITE, designated SEQ ID:25218, to the nucleotide sequence of

VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46101] Another function of VGAM1303 is therefore inhibition of DKFZP434J037 (Accession NM_030952). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J037. DKFZP564J157 (Accession NM_018457) is another VGAM1303 host target gene. DKFZP564J157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564J157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564J157 BINDING SITE, designated SEQ ID:20528, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46102] Another function of VGAM1303 is therefore inhibition of DKFZP564J157 (Accession NM_018457). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564J157. DQX1 (Accession NM_133637) is another VGAM1303 host target gene. DQX1 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DQX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DQX1 BINDING SITE, designated SEQ ID:28598, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46103] Another function of VGAM1303 is therefore inhibition of DQX1 (Accession NM_133637). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DQX1. FLJ10922 (Accession NM_018273) is another VGAM1303 host target gene. FLJ10922 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10922 BINDING SITE, designated SEQ ID:20254, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46104] Another function of VGAM1303 is therefore inhibition of

FLJ10922 (Accession NM_018273). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10922. FLJ13769 (Accession NM_025012) is another VGAM1303 host target gene. FLJ13769 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13769 BINDING SITE, designated SEQ ID:24593, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46105] Another function of VGAM1303 is therefore inhibition of FLJ13769 (Accession NM_025012). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13769. KIAA1691 (Accession XM_166523) is another VGAM1303 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44468, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46106] Another function of VGAM1303 is therefore inhibition of KIAA1691 (Accession XM_166523). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. Leucine-rich Repeat LGI Family, Member 2 (LGI2, Accession NM_018176) is another VGAM1303 host target gene. LGI2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LGI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LGI2 BINDING SITE, designated SEQ ID:20000, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46107] Another function of VGAM1303 is therefore inhibition of Leucine-rich Repeat LGI Family, Member 2 (LGI2, Accession NM_018176). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with LGI2. Paired Mesoderm Homeobox 2b (PMX2B, Accession NM_003924) is another VGAM1303 host target gene. PMX2B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PMX2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMX2B BINDING SITE, designated SEQ ID:10017, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46108] Another function of VGAM1303 is therefore inhibition of Paired Mesoderm Homeobox 2b (PMX2B, Accession NM_003924). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMX2B. LOC144438 (Accession XM_084860) is another VGAM1303 host target gene. LOC144438 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144438 BINDING SITE, desig-

nated SEQ ID:37735, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46109] Another function of VGAM1303 is therefore inhibition of LOC144438 (Accession XM_084860). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144438. LOC147804 (Accession XM_085901) is another VGAM1303 host target gene. LOC147804 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147804, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147804 BINDING SITE, designated SEQ ID:38382, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46110] Another function of VGAM1303 is therefore inhibition of LOC147804 (Accession XM_085901). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147804. LOC148759 (Accession XM_097517) is another VGAM1303 host target gene. LOC148759 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148759 BINDING SITE, designated SEQ ID:40903, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46111] Another function of VGAM1303 is therefore inhibition of LOC148759 (Accession XM_097517). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148759. LOC253219 (Accession XM_173743) is another VGAM1303 host target gene. LOC253219 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253219 BINDING SITE, designated SEQ ID:46561, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46112] Another function of VGAM1303 is therefore inhibition of

LOC253219 (Accession XM_173743). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253219. LOC257358 (Accession XM_173138) is another VGAM1303 host target gene. LOC257358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257358 BINDING SITE, designated SEQ ID:46388, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46113] Another function of VGAM1303 is therefore inhibition of LOC257358 (Accession XM_173138). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257358. LOC91759 (Accession XM_040467) is another VGAM1303 host target gene. LOC91759 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC91759 BINDING SITE, designated SEQ ID:33304, to the nucleotide sequence of VGAM1303 RNA, herein designated VGAM RNA, also designated SEQ ID:4014.

[46114] Another function of VGAM1303 is therefore inhibition of LOC91759 (Accession XM_040467). Accordingly, utilities of VGAM1303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91759. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1304 (VGAM1304) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46115] VGAM1304 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1304 was detected is described hereinabove with reference to Figs. 1–8.

[46116] VGAM1304 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[46117] VGAM1304 gene encodes a VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1304 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1304 precursor RNA is designated SEQ ID:1290, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1290 is located at position 179588 relative to the genome of Human Herpesvirus 5.

[46118] VGAM1304 precursor RNA folds onto itself, forming VGAM1304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46119] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1304 folded precursor RNA into VGAM1304 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1304 RNA is designated SEQ ID:4015, and is provided hereinbelow with reference to the sequence listing part.

[46120] VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1304 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46121] VGAM1304 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1304 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1304 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46122] The complementary binding of VGAM1304 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1304 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1304 host target RNA into VGAM1304 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46123] It is appreciated that VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1304 host target genes. The mRNA of each one of this plurality of VGAM1304 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1304 RNA, herein designated VGAM RNA, and which when bound by VGAM1304 RNA causes inhibition of translation of respective one or more VGAM1304 host target proteins.

[46124] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1304 gene, herein designated VGAM GENE, on one or more VGAM1304 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46125] It is yet further appreciated that a function of VGAM1304 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1304 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM1304 correlate with, and may be deduced from, the identity of the host target genes which VGAM1304 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46126] Nucleotide sequences of the VGAM1304 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1304 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1304 are further described hereinbelow with reference to Table 1.

[46127] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1304 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1304 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46128] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1304 gene, herein designated VGAM is inhibition of expression of VGAM1304 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1304 correlate with, and may be deduced from, the identity of the target genes which VGAM1304 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46129] Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717) is a VGAM1304 host target gene. DGKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKI BINDING SITE, designated SEQ ID:11078, to the nucleotide sequence of VGAM1304 RNA, herein designated VGAM RNA, also designated SEQ ID:4015.

[46130] A function of VGAM1304 is therefore inhibition of Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717), a gene which regulates the intracellular concentration of the second messenger diacylglycerol (DAG). Accordingly, utilities of VGAM1304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKI. The function of DGKI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1107. DKFZp547J036 (Accession NM_032281) is another VGAM1304 host target gene. DKFZp547J036 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547J036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547J036 BINDING SITE, designated SEQ ID:26039, to the nucleotide sequence of VGAM1304 RNA, herein designated VGAM RNA, also designated SEQ ID:4015.

[46131] Another function of VGAM1304 is therefore inhibition of DKFZp547J036 (Accession NM_032281). Accordingly, utilities of VGAM1304 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp547J036. KIAA0872 (Accession NM_014940) is another VGAM1304 host target gene. KIAA0872 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0872 BINDING SITE, designated SEQ ID:17242, to the nucleotide sequence of VGAM1304 RNA, herein designated VGAM RNA, also designated SEQ ID:4015.

[46132] Another function of VGAM1304 is therefore inhibition of KIAA0872 (Accession NM_014940). Accordingly, utilities of VGAM1304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0872. KIAA1979 (Accession XM_113984) is another VGAM1304 host target gene. KIAA1979 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1979 BINDING SITE, designated SEQ ID:42589, to the

nucleotide sequence of VGAM1304 RNA, herein designated VGAM RNA, also designated SEQ ID:4015.

[46133] Another function of VGAM1304 is therefore inhibition of KIAA1979 (Accession XM_113984). Accordingly, utilities of VGAM1304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1305 (VGAM1305) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46134] VGAM1305 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1305 was detected is described hereinabove with reference to Figs. 1–8.

[46135] VGAM1305 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46136] VGAM1305 gene encodes a VGAM1305 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1305 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1305 precursor RNA is designated SEQ ID:1291, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1291 is located at position 409 relative to the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2).

- [46137] VGAM1305 precursor RNA folds onto itself, forming VGAM1305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46138] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1305 folded precursor RNA into VGAM1305 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1305 RNA is designated SEQ ID:4016, and is provided hereinbelow with reference to the sequence listing part.

[46139] VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1305 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46140] VGAM1305 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1305 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1305 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46141] The complementary binding of VGAM1305 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1305 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1305 host target RNA into VGAM1305 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46142] It is appreciated that VGAM1305 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1305 host target genes. The mRNA of each one of this plurality of VGAM1305 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1305 RNA, herein designated VGAM RNA, and which when bound by VGAM1305 RNA causes inhibition of translation of respective one or more VGAM1305 host target proteins.

[46143] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1305 gene, herein designated VGAM GENE, on one or more VGAM1305 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[46144] It is yet further appreciated that a function of VGAM1305 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). Specific functions, and accordingly utilities, of VGAM1305 correlate with, and may be deduced from, the identity of the host target genes which VGAM1305 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46145] Nucleotide sequences of the VGAM1305 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1305 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1305 are further described hereinbelow with reference to Table 1.

[46146] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1305 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1305 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46147] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1305 gene, herein designated VGAM is inhibition of expression of VGAM1305 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1305 correlate with, and may be deduced from, the identity of the target genes which VGAM1305 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46148] Checkpoint Suppressor 1 (CHES1, Accession NM_005197) is a VGAM1305 host target gene. CHES1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHES1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHES1 BINDING SITE, designated SEQ ID:11697, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46149] A function of VGAM1305 is therefore inhibition of Check-

point Suppressor 1 (CHES1, Accession NM_005197). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHES1. Coagulation Factor C Homolog, Cochlin (*Limulus polyphemus*) (COCH, Accession NM_004086) is another VGAM1305 host target gene. COCH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COCH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COCH BINDING SITE, designated SEQ ID:10292, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46150] Another function of VGAM1305 is therefore inhibition of Coagulation Factor C Homolog, Cochlin (*Limulus polyphemus*) (COCH, Accession NM_004086). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COCH. Dachshund Homolog (*Drosophila*) (DACH, Accession NM_080759) is another VGAM1305 host target gene. DACH BINDING SITE is HOST TARGET binding site found in

the 3` untranslated region of mRNA encoded by DACH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DACH BINDING SITE, designated SEQ ID:28034, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46151] Another function of VGAM1305 is therefore inhibition of Dachshund Homolog (Drosophila) (DACH, Accession NM_080759), a gene which regulates early progenitor cell proliferation during retinogenesis and pituitary development . Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DACH. The function of DACH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM260. Inositol Polyphosphate-5-phosphatase, 40kDa (INPP5A, Accession NM_005539) is another VGAM1305 host target gene. INPP5A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by INPP5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of INPP5A BINDING SITE, designated SEQ ID:12066, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46152] Another function of VGAM1305 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 40kDa (INPP5A, Accession NM_005539), a gene which hydrolyzes the calcium-mobilizing second messenger $\text{ins}(1,4,5)\text{p}3$. Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5A. The function of INPP5A has been established by previous studies. The phosphatidylinositols serve as precursors for a number of different messenger molecules. Agonist stimulation of cells results in phosphatidylinositol turnover and the generation of inositol 1,4,5-triphosphate, $\text{Ins}(1,4,5)\text{P}3$, which mobilizes intracellular calcium. The inositol polyphosphate-5-phosphatase enzymes hydrolyze $\text{Ins}(1,4,5)\text{P}3$ in a signal-terminating reaction. Laxminarayan et al. (1994) isolated a 2.7-kb composite cDNA encoding the 43-kD membrane-associated 5-phosphatase by screening a human placental lambda-gt11 library using degenerate

oligonucleotides. The 2.7-kb cDNA contained a 1.1-kb open reading frame, comprising 363 amino acids, which encoded a protein of predicted molecular mass of 42 kD. They showed that a 73-amino acid domain in the COOH terminus of the 43-kD membrane-associated 5-phosphatase had 30% sequence identity and 67% similarity to a region in the 75-kD 5-phosphatase (OMIM Ref. No. 147264) and 34% identity and 70% similarity to a sequence in the protein that is encoded by the gene defective in Lowe oculocerebral renal syndrome (OMIM Ref. No. 309000). The 43-kD membrane-associated 5-phosphatase appeared to be predominantly expressed in heart, brain, and skeletal muscle.

[46153] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46154] Laxminarayan, K. M.; Chan, B. K.; Tetaz, T.; Bird, P. I.; Mitchell, C. A. : Characterization of a cDNA encoding the 43-kDa membrane-associated inositol-polyphosphate 5-phosphatase. J. Biol. Chem. 269: 17305-17310, 1994. ; and

[46155] Mitchell, C. A.; Speed, C. J.; Nicholl, J.; Sutherland, G. R. : Chromosomal mapping of the gene (INPP5A) encoding the

43-kDa membrane-associated inositol polyphosphate 5-phosphatase to 1.

[46156] Further studies establishing the function and utilities of INPP5A are found in John Hopkins OMIM database record ID 600106, and in cited publications numbered 878 and 8792 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nucleoporin 98kDa (NUP98, Accession NM_016320) is another VGAM1305 host target gene. NUP98 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NUP98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP98 BINDING SITE, designated SEQ ID:18442, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46157] Another function of VGAM1305 is therefore inhibition of Nucleoporin 98kDa (NUP98, Accession NM_016320), a gene which functions in the nuclear transport of protein and RNA. Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP98. The function of NUP98

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.RAP1, GTPase Activating Protein 1 (RAP1GA1, Accession NM_002885) is another VGAM1305 host target gene. RAP1GA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAP1GA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP1GA1 BINDING SITE, designated SEQ ID:8797, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46158] Another function of VGAM1305 is therefore inhibition of RAP1, GTPase Activating Protein 1 (RAP1GA1, Accession NM_002885). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP1GA1. Son of Sevenless Homolog 2 (Drosophila) (SOS2, Accession XM_043720) is another VGAM1305 host target gene. SOS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SOS2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOS2 BINDING SITE, designated SEQ ID:33999, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46159] Another function of VGAM1305 is therefore inhibition of Son of Sevenless Homolog 2 (Drosophila) (SOS2, Accession XM_043720). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOS2. Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM_024331) is another VGAM1305 host target gene. C20orf121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf121 BINDING SITE, designated SEQ ID:23630, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46160] Another function of VGAM1305 is therefore inhibition of

Chromosome 20 Open Reading Frame 121 (C20orf121, Accession NM_024331). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf121. E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM_001421) is another VGAM1305 host target gene. ELF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ELF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF4 BINDING SITE, designated SEQ ID:7121, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46161] Another function of VGAM1305 is therefore inhibition of E74-like Factor 4 (ets domain transcription factor) (ELF4, Accession NM_001421). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF4. KIAA0218 (Accession NM_014760) is another VGAM1305 host target gene. KIAA0218 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by KIAA0218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0218 BINDING SITE, designated SEQ ID:16516, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46162] Another function of VGAM1305 is therefore inhibition of KIAA0218 (Accession NM_014760). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0218. KIAA0889 (Accession NM_015377) is another VGAM1305 host target gene. KIAA0889 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0889, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0889 BINDING SITE, designated SEQ ID:17676, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46163] Another function of VGAM1305 is therefore inhibition of KIAA0889 (Accession NM_015377). Accordingly, utilities

of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0889. KIAA0945 (Accession NM_014952) is another VGAM1305 host target gene. KIAA0945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0945 BINDING SITE, designated SEQ ID:17294, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46164] Another function of VGAM1305 is therefore inhibition of KIAA0945 (Accession NM_014952). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0945. KIAA1198 (Accession XM_032674) is another VGAM1305 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1198 BINDING SITE, designated SEQ ID:31707, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46165] Another function of VGAM1305 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. MGC2827 (Accession NM_023940) is another VGAM1305 host target gene. MGC2827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2827 BINDING SITE, designated SEQ ID:23424, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46166] Another function of VGAM1305 is therefore inhibition of MGC2827 (Accession NM_023940). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2827. TRIP-Br2 (Accession NM_014755) is another VGAM1305 host target gene. TRIP-Br2 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIP-Br2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16484, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46167] Another function of VGAM1305 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. LOC115110 (Accession XM_049825) is another VGAM1305 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115110 BINDING SITE, designated SEQ ID:35507, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46168] Another function of VGAM1305 is therefore inhibition of

LOC115110 (Accession XM_049825). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115110. LOC149506 (Accession XM_097661) is another VGAM1305 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41005, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46169] Another function of VGAM1305 is therefore inhibition of LOC149506 (Accession XM_097661). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149506. LOC152317 (Accession XM_098189) is another VGAM1305 host target gene. LOC152317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC152317 BINDING SITE, designated SEQ ID:41466, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46170] Another function of VGAM1305 is therefore inhibition of LOC152317 (Accession XM_098189). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152317. LOC163882 (Accession XM_089211) is another VGAM1305 host target gene. LOC163882 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163882 BINDING SITE, designated SEQ ID:39971, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46171] Another function of VGAM1305 is therefore inhibition of LOC163882 (Accession XM_089211). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163882. LOC253148 (Accession XM_173032) is an-

other VGAM1305 host target gene. LOC253148 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253148, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253148 BINDING SITE, designated SEQ ID:46299, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46172] Another function of VGAM1305 is therefore inhibition of LOC253148 (Accession XM_173032). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253148. LOC90072 (Accession XM_028702) is another VGAM1305 host target gene. LOC90072 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90072 BINDING SITE, designated SEQ ID:30727, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46173] Another function of VGAM1305 is therefore inhibition of LOC90072 (Accession XM_028702). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90072. LOC90630 (Accession XM_033046) is another VGAM1305 host target gene. LOC90630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90630 BINDING SITE, designated SEQ ID:31825, to the nucleotide sequence of VGAM1305 RNA, herein designated VGAM RNA, also designated SEQ ID:4016.

[46174] Another function of VGAM1305 is therefore inhibition of LOC90630 (Accession XM_033046). Accordingly, utilities of VGAM1305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90630. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1306 (VGAM1306) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[46175] VGAM1306 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1306 was detected is described hereinabove with reference to Figs. 1–8.

[46176] VGAM1306 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV–SAT2). VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46177] VGAM1306 gene encodes a VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1306 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1306 precursor RNA is designated SEQ ID:1292, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1292 is located at position 4577 relative to the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV–SAT2).

[46178] VGAM1306 precursor RNA folds onto itself, forming

VGAM1306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46179] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1306 folded precursor RNA into VGAM1306 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1306 RNA is designated SEQ ID:4017, and is provided hereinbelow with reference to the sequence listing part.

[46180] VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1306 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46181] VGAM1306 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1306 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1306 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46182] The complementary binding of VGAM1306 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1306 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1306 host target RNA into VGAM1306 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46183] It is appreciated that VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1306 host target genes. The mRNA of each one of this plurality of VGAM1306 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1306 RNA, herein designated VGAM RNA, and which when bound by VGAM1306 RNA causes inhibition of translation of respective one or more VGAM1306 host target proteins.

[46184] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1306 gene, herein designated VGAM GENE, on one or more VGAM1306 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46185] It is yet further appreciated that a function of VGAM1306 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). Specific functions, and accordingly utilities, of VGAM1306 correlate with, and may be deduced from, the identity of the host target genes which

VGAM1306 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46186] Nucleotide sequences of the VGAM1306 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1306 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1306 are further described hereinbelow with reference to Table 1.

[46187] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1306 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1306 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46188] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1306 gene, herein designated VGAM is inhibition of expression of VGAM1306 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1306 correlate with, and may be deduced from, the identity of the target genes which VGAM1306 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[46189] Alcohol Dehydrogenase 7 (class IV), Mu Or Sigma Polypeptide (ADH7, Accession NM_000673) is a VGAM1306 host target gene. ADH7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADH7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADH7 BINDING SITE, designated SEQ ID:6326, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46190] A function of VGAM1306 is therefore inhibition of Alcohol Dehydrogenase 7 (class IV), Mu Or Sigma Polypeptide (ADH7, Accession NM_000673), a gene which retinol oxidation for the synthesis of retinoic acid, a hormone important for cellular differentiation. Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADH7. The function of ADH7 has been established by previous studies. Satre et al. (1994) characterized a novel human alcohol dehydrogenase gene called ADH7 and determined that it encodes a class IV ADH that is very active as a

retinol dehydrogenase. They isolated a nearly full-length cDNA for ADH7 from a human stomach cDNA library and a 5-prime genomic clone containing exons 1 and 2 from a human genomic library. The deduced full-length amino acid sequence predicted a protein of 373 amino acids following the initiator methionine. The class IV identity of the sequence was confirmed by agreement with previously determined sequences for several human stomach class IV ADH peptides. Sequence comparison suggested that human ADH classes I and IV may have diverged from a common ancestor after the separation of the other classes, and may still share common physiologic functions. Satre et al. (1994) discussed the possibility that one of these functions is retinol oxidation for the synthesis of retinoic acid, a hormone important for cellular differentiation. Zgombic-Knight et al. (1995) demonstrated that the ADH7 gene has 9 exons and encodes a predicted polypeptide of 373 amino acids, excluding the amino-terminal methionine. ADH7 showed greater sequence identity with class I ADH (69%) than with classes II (e.g., 103740), III (e.g., 103710), or V, with which it is only 59–61% homologous. Zgombic-Knight et al. (1995) confirmed that ADH7 is the major stomach ADH, but, unlike the others, is absent from

liver. Also, transcriptional regulation of the ADH7 gene appeared to be different from that of the other classes in that the ADH7 promoter lacks a TATA box and GC boxes upstream of the transcription initiation site. As outlined by Osier et al. (2002), 7 genes encoding ADH enzymes exist in a cluster extending approximately 380 kb on the long arm of chromosome 4. The class I ADH genes exist in a tighter cluster of approximately 77 kb, flanked upstream by ADH7 and downstream by ADH6 (OMIM Ref. No. 103735), ADH4 (OMIM Ref. No. 103740), and ADH5 (OMIM Ref. No. 103710), in that order.

[46191] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46192] Zgombic-Knight, M.; Foglio, M. H.; Duester, G. : Genomic structure and expression of the ADH7 gene encoding human class IV alcohol dehydrogenase, the form most efficient for retinol metabolism in vitro. J. Biol. Chem. 270: 4305-4311, 1995. ; and

[46193] Osier, M. V.; Pakstis, A. J.; Soodyall, H.; Comas, D.; Goldman, D.; Odunsi, A.; Okonofua, F.; Parnas, J.; Schulz, L. O.; Bertranpetit, J.; Bonne-Tamir, B.; Lu, R.-B.; Kidd, J. R.; Kidd.

[46194] Further studies establishing the function and utilities of ADH7 are found in John Hopkins OMIM database record ID 600086, and in cited publications numbered 12102–7899 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MADS Box Transcription Enhancer Factor 2, Polypeptide D (myocyte enhancer factor 2D) (MEF2D, Accession XM_173049) is another VGAM1306 host target gene. MEF2D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEF2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2D BINDING SITE, designated SEQ ID:46308, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46195] Another function of VGAM1306 is therefore inhibition of MADS Box Transcription Enhancer Factor 2, Polypeptide D (myocyte enhancer factor 2D) (MEF2D, Accession XM_173049), a gene which regulates muscle-specific and mitogen-inducible genes. Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF2D.

The function of MEF2D has been established by previous studies. The MEF2 family of regulatory proteins are, like the myogenic basic helix–loop–helix proteins (see OMIM Ref. No. 159970), involved in myogenesis; see (OMIM Ref. No. 600660). Breitbart et al. (1993) obtained MEF2D cDNAs from an adult cardiac ventricle expression library screened at low stringency with a human MEF2B probe. One of the cDNAs encoded a 521–amino acid protein with highly conserved MADS and MEF2 domains. The recombinantly expressed MEF2D protein showed DNA binding to the MEF2 site. Breitbart et al. (1993) found that MEF2D occurs as several alternatively spliced transcripts, one of which resembles the *Xenopus* SRF–related factor SL–1. Unlike the other MEF2 family members, MEF2D is present in undifferentiated myoblasts and may participate in the earliest stages of commitment. Hobson et al. (1995) mapped the MEF2D gene to 1q12–q23 using somatic cell hybrid panel DNAs containing deletion or derivative chromosomes. Mouse Mef2D was mapped by Martin et al. (1994) to chromosome 3. Ikeshima et al. (1995) demonstrated strong expression of MEF2D in the cerebellum and cerebrum of developing mouse brains and also in central nervous system neurons of adult mice, suggesting that it

may be involved in the differentiation of neurogenic as well as myogenic cells.

[46196] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46197] Hobson, G. M.; Krahe, R.; Garcia, E.; Siciliano, M. J.; Funanage, V. L. : Regional chromosomal assignments for four members of the MADS domain transcription enhancer factor 2 (MEF2) gene family to human chromosomes 15q26, 19p12, 5q14, and 1q12–q23. *Genomics* 29: 704–711, 1995. ; and

[46198] Ikeshima, H.; Imai, S.; Shimoda, K.; Hata, J.; Takano, T. : Expression of a MADS box gene, MEF2D, in neurons of the mouse central nervous system: implication of its binary function in m.

[46199] Further studies establishing the function and utilities of MEF2D are found in John Hopkins OMIM database record ID 600663, and in cited publications numbered 8293–8294, 817 and 8296 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM1306 host target gene. WHSC1 BINDING SITE1 through WHSC1

BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28442, SEQ ID:28459 and SEQ ID:17178 respectively, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46200] Another function of VGAM1306 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. KIAA1276 (Accession XM_039169) is another VGAM1306 host target gene. KIAA1276 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1276, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1276 BINDING SITE, designated SEQ ID:33019, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46201] Another function of VGAM1306 is therefore inhibition of KIAA1276 (Accession XM_039169). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1276. PRO0800 (Accession NM_018592) is another VGAM1306 host target gene. PRO0800 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0800 BINDING SITE, designated SEQ ID:20671, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46202] Another function of VGAM1306 is therefore inhibition of PRO0800 (Accession NM_018592). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PRO0800. LOC148266 (Accession XM_086128) is another VGAM1306 host target gene. LOC148266 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148266 BINDING SITE, designated SEQ ID:38513, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46203] Another function of VGAM1306 is therefore inhibition of LOC148266 (Accession XM_086128). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148266. LOC151009 (Accession XM_097992) is another VGAM1306 host target gene. LOC151009 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151009 BINDING SITE, designated SEQ ID:41290, to

the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46204] Another function of VGAM1306 is therefore inhibition of LOC151009 (Accession XM_097992). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151009. LOC157660 (Accession XM_098805) is another VGAM1306 host target gene. LOC157660 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157660, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157660 BINDING SITE, designated SEQ ID:41829, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46205] Another function of VGAM1306 is therefore inhibition of LOC157660 (Accession XM_098805). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157660. LOC170409 (Accession XM_096330) is another VGAM1306 host target gene. LOC170409 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC170409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170409 BINDING SITE, designated SEQ ID:40317, to the nucleotide sequence of VGAM1306 RNA, herein designated VGAM RNA, also designated SEQ ID:4017.

[46206] Another function of VGAM1306 is therefore inhibition of LOC170409 (Accession XM_096330). Accordingly, utilities of VGAM1306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1307 (VGAM1307) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46207] VGAM1307 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1307 was detected is described hereinabove with reference to Figs. 1-8.

[46208] VGAM1307 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46209] VGAM1307 gene encodes a VGAM1307 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1307 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1307 precursor RNA is designated SEQ ID:1293, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1293 is located at position 5733 relative to the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2).

[46210] VGAM1307 precursor RNA folds onto itself, forming VGAM1307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[46211] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1307 folded precursor RNA into VGAM1307 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1307 RNA is designated SEQ ID:4018, and is provided hereinbelow with reference to the sequence listing part.

[46212] VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1307 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46213] VGAM1307 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1307 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1307 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1307 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[46214] The complementary binding of VGAM1307 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1307 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1307 host target RNA into VGAM1307 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46215] It is appreciated that VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1307 host target genes. The mRNA of each one of this plurality of VGAM1307 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1307 RNA, herein designated VGAM RNA, and which when bound by VGAM1307 RNA causes inhibition of translation of respective one or more VGAM1307 host target proteins.

[46216] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1307 gene, herein designated VGAM GENE, on one or more VGAM1307 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46217] It is yet further appreciated that a function of VGAM1307 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). Specific functions, and accordingly utilities, of VGAM1307 correlate with, and may be deduced from, the identity of the host target genes which VGAM1307 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46218] Nucleotide sequences of the VGAM1307 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1307 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1307 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1307 are further described hereinbelow with reference to Table 1.

[46219] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1307 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1307 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46220] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1307 gene, herein designated VGAM is inhibition of expression of VGAM1307 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1307 correlate with, and may be deduced from, the identity of the target genes which VGAM1307 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46221] Growth Arrest-specific 11 (GAS11, Accession NM_001481) is a VGAM1307 host target gene. GAS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of GAS11 BINDING SITE, designated SEQ ID:7219, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46222] A function of VGAM1307 is therefore inhibition of Growth Arrest-specific 11 (GAS11, Accession NM_001481). Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS11. LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055) is another VGAM1307 host target gene. LANCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANCL1 BINDING SITE, designated SEQ ID:12695, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46223] Another function of VGAM1307 is therefore inhibition of LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055), a gene which

binds the C-terminus of stomatin. Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANCL1. The function of LANCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM656. Microtubule-associated Protein Tau (MAPT, Accession NM_016835) is another VGAM1307 host target gene. MAPT BINDING SITE1 through MAPT BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPT BINDING SITE1 through MAPT BINDING SITE4, designated SEQ ID:18831, SEQ ID:18837, SEQ ID:12537 and SEQ ID:18825 respectively, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46224] Another function of VGAM1307 is therefore inhibition of Microtubule-associated Protein Tau (MAPT, Accession NM_016835), a gene which Microtubule-associated protein tau; promotes microtubule assembly. Accordingly,

utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPT. The function of MAPT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Neurexin 2 (NRXN2, Accession NM_138732) is another VGAM1307 host target gene. NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3, designated SEQ ID:28984, SEQ ID:17468 and SEQ ID:42767 respectively, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46225] Another function of VGAM1307 is therefore inhibition of Neurexin 2 (NRXN2, Accession NM_138732), a gene which may be involved in cell recognition, cell adhesion, and may mediate intracellular signaling. Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

NRXN2. The function of NRXN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.FLJ10829 (Accession NM_018234) is another VGAM1307 host target gene. FLJ10829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10829 BINDING SITE, designated SEQ ID:20177, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46226] Another function of VGAM1307 is therefore inhibition of FLJ10829 (Accession NM_018234). Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10829. KIAA0923 (Accession NM_014021) is another VGAM1307 host target gene. KIAA0923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0923 BINDING SITE, designated SEQ ID:15243, to the nucleotide sequence of VGAM1307 RNA, herein designated VGAM RNA, also designated SEQ ID:4018.

[46227] Another function of VGAM1307 is therefore inhibition of KIAA0923 (Accession NM_014021). Accordingly, utilities of VGAM1307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0923. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1308 (VGAM1308) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46228] VGAM1308 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1308 was detected is described hereinabove with reference to Figs. 1–8.

[46229] VGAM1308 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV–SAT2). VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, is a

human gene contained in the human genome.

[46230] VGAM1308 gene encodes a VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1308 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1308 precursor RNA is designated SEQ ID:1294, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1294 is located at position 4790 relative to the genome of Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2).

[46231] VGAM1308 precursor RNA folds onto itself, forming VGAM1308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46232] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1308 folded precursor RNA into VGAM1308

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1308 RNA is designated SEQ ID:4019, and is provided hereinbelow with reference to the sequence listing part.

[46233] VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1308 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46234] VGAM1308 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1308 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1308 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46235] The complementary binding of VGAM1308 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1308 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1308 host target RNA into VGAM1308 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[46236] It is appreciated that VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1308 host target genes. The mRNA of each one of this plurality of VGAM1308 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1308 RNA, herein designated VGAM RNA, and which when bound by VGAM1308 RNA causes inhibition of translation of respective one or more VGAM1308 host target proteins.

[46237] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1308 gene, herein designated VGAM GENE, on one or more VGAM1308 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46238] It is yet further appreciated that a function of VGAM1308 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). Specific functions, and accordingly utilities, of VGAM1308 correlate with, and may be deduced from, the identity of the host target genes which VGAM1308 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46239] Nucleotide sequences of the VGAM1308 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1308 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1308 are further described hereinbelow with reference to Table 1.

[46240] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1308 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1308 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46241] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1308 gene, herein designated VGAM is inhibition of expression of VGAM1308 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1308 correlate with, and may be deduced from, the identity of the target genes which VGAM1308 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46242] Aprataxin (APTX, Accession NM_017692) is a VGAM1308 host target gene. APTX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APTX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APTX BINDING SITE, designated SEQ ID:19250, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ

ID:4019.

[46243] A function of VGAM1308 is therefore inhibition of Aprataxin (APTX, Accession NM_017692). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APTX. CERD4 (Accession NM_012074) is another VGAM1308 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14350, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46244] Another function of VGAM1308 is therefore inhibition of CERD4 (Accession NM_012074). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. G Protein-coupled Receptor Kinase 6 (GPRK6, Accession NM_002082) is another VGAM1308 host target gene. GPRK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPRK6,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRK6 BINDING SITE, designated SEQ ID:7877, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46245] Another function of VGAM1308 is therefore inhibition of G Protein-coupled Receptor Kinase 6 (GPRK6, Accession NM_002082), a gene which regulates the G protein-coupled receptors. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRK6. The function of GPRK6 has been established by previous studies. By PCR on neutrophil cDNA using primers based on sequences of known receptor kinases, Haribabu and Snyderman (1993) identified GPRK5 (OMIM Ref. No. 600870) and GPRK6 sequences. Using a fragment of the GPRK6 PCR clone to screen a cDNA library, they isolated a cDNA encoding GPRK6. Sequence analysis predicted that the 544-amino acid GPRK6 protein contains the conserved DLG (asp-leu-gly) and ENIL (glu-asn-ile-leu) motifs. Northern blot analysis detected 2.1- and 2.9-kb GPRK6 transcripts in all tissues tested, with strongest expression in placenta

and skeletal muscle. By somatic cell hybrid analysis, Haribabu and Snyderman (1993) mapped the GPRK6 gene and a closely related gene to chromosomes 5 and 13, respectively. Bullrich et al. (1995) mapped GPRK6 to 5q35 by analysis of a rodent human hybrid panel. The GPRK6-related locus was found to map to 13pter-q21.

[46246] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46247] Bullrich, F.; Druck, T.; Kunapuli, P.; Gomez, J.; Gripp, K. W.; Schlegelberger, B.; Lasota, J.; Aronson, M.; Cannizzaro, L. A.; Huebner, K.; Benovic, J. L. : Chromosomal mapping of the genes GPRK5 and GPRK6 encoding G protein-coupled receptor kinases GRK5 and GRK6. *Cytogenet. Cell Genet.* 70: 250-254, 1995. ; and

[46248] Haribabu, B.; Snyderman, R. : Identification of additional members of human G-protein-coupled receptor kinase multigene family. *Proc. Nat. Acad. Sci.* 90: 9398-9402, 1993.

[46249] Further studies establishing the function and utilities of GPRK6 are found in John Hopkins OMIM database record ID 600869, and in cited publications numbered 7022-7023 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM_096169) is another VGAM1308 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40303, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46250] Another function of VGAM1308 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 145kDa (INPP5D, Accession XM_096169), a gene which hydrolyzes Ins(1,3,4,5)P₄ and PtdIns(3,4,5)P₃; contains an SH2-domain. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM64.Mab-21-like 1 (*C. elegans*) (MAB21L1, Accession

NM_005584) is another VGAM1308 host target gene. MAB21L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAB21L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L1 BINDING SITE, designated SEQ ID:12112, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46251] Another function of VGAM1308 is therefore inhibition of Mab-21-like 1 (*C. elegans*) (MAB21L1, Accession NM_005584), a gene which may control cerebellum and eye development; very strongly similar to murine Mm.10798. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L1. The function of MAB21L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM39. Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM_002734) is another VGAM1308 host target

gene. PRKAR1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRKAR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR1A BINDING SITE, designated SEQ ID:8607, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46252] Another function of VGAM1308 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type I, Alpha (tissue specific extinguisher 1) (PRKAR1A, Accession NM_002734). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR1A. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063) is another VGAM1308 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11495, to the nu-

cleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46253] Another function of VGAM1308 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660) is another VGAM1308 host target gene. TGFB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TGFB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB1 BINDING SITE, designated SEQ ID:6320, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46254] Another function of VGAM1308 is therefore inhibition of

Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB1. Zinc Finger Protein 236 (ZNF236, Accession NM_007345) is another VGAM1308 host target gene. ZNF236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF236 BINDING SITE, designated SEQ ID:14275, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46255] Another function of VGAM1308 is therefore inhibition of Zinc Finger Protein 236 (ZNF236, Accession NM_007345). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF236. Cyclin M4 (CNNM4, Accession NM_020184) is another VGAM1308 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CNNM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM4 BINDING SITE, designated SEQ ID:21424, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46256] Another function of VGAM1308 is therefore inhibition of Cyclin M4 (CNNM4, Accession NM_020184). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM4. DDM36 (Accession NM_020962) is another VGAM1308 host target gene. DDM36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDM36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDM36 BINDING SITE, designated SEQ ID:21951, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46257] Another function of VGAM1308 is therefore inhibition of DDM36 (Accession NM_020962). Accordingly, utilities of

VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDM36. DKFZp761B0514 (Accession NM_032289) is another VGAM1308 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26049, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46258] Another function of VGAM1308 is therefore inhibition of DKFZp761B0514 (Accession NM_032289). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B0514. Fibroblast Growth Factor 19 (FGF19, Accession NM_005117) is another VGAM1308 host target gene. FGF19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF19 BINDING SITE, designated SEQ ID:11595, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46259] Another function of VGAM1308 is therefore inhibition of Fibroblast Growth Factor 19 (FGF19, Accession NM_005117). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF19. FLJ12547 (Accession NM_024992) is another VGAM1308 host target gene. FLJ12547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12547 BINDING SITE, designated SEQ ID:24546, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46260] Another function of VGAM1308 is therefore inhibition of FLJ12547 (Accession NM_024992). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12547. KIAA0296 (Accession NM_014699) is another VGAM1308 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16219, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46261] Another function of VGAM1308 is therefore inhibition of KIAA0296 (Accession NM_014699). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. KIAA0523 (Accession XM_041964) is another VGAM1308 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33640, to the

nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46262] Another function of VGAM1308 is therefore inhibition of KIAA0523 (Accession XM_041964). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. KIAA1297 (Accession XM_051005) is another VGAM1308 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35720, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46263] Another function of VGAM1308 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KREMEN (Accession NM_032045) is another VGAM1308 host target gene. KREMEN BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KREMEN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KREMEN BINDING SITE, designated SEQ ID:25759, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46264] Another function of VGAM1308 is therefore inhibition of KREMEN (Accession NM_032045). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KREMEN. MGC5457 (Accession NM_032633) is another VGAM1308 host target gene. MGC5457 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5457 BINDING SITE, designated SEQ ID:26347, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46265] Another function of VGAM1308 is therefore inhibition of MGC5457 (Accession NM_032633). Accordingly, utilities

of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5457. Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007) is another VGAM1308 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34881, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46266] Another function of VGAM1308 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. PRO1430 (Accession NM_018599) is another VGAM1308 host target gene. PRO1430 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1430 BINDING SITE, designated SEQ ID:20677, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46267] Another function of VGAM1308 is therefore inhibition of PRO1430 (Accession NM_018599). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1430. LOC130951 (Accession NM_138804) is another VGAM1308 host target gene. LOC130951 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130951 BINDING SITE, designated SEQ ID:29027, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46268] Another function of VGAM1308 is therefore inhibition of LOC130951 (Accession NM_138804). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC130951. LOC201324 (Accession XM_043753) is another VGAM1308 host target gene. LOC201324 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201324, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201324 BINDING SITE, designated SEQ ID:34013, to the nucleotide sequence of VGAM1308 RNA, herein designated VGAM RNA, also designated SEQ ID:4019.

[46269] Another function of VGAM1308 is therefore inhibition of LOC201324 (Accession XM_043753). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201324. LOC256021 (Accession XM_172884) is another VGAM1308 host target gene. LOC256021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256021 BINDING SITE, designated SEQ ID:46166, to the nucleotide sequence of VGAM1308 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4019.

[46270] Another function of VGAM1308 is therefore inhibition of LOC256021 (Accession XM_172884). Accordingly, utilities of VGAM1308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256021. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1309 (VGAM1309) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46271] VGAM1309 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1309 was detected is described hereinabove with reference to Figs. 1–8.

[46272] VGAM1309 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46273] VGAM1309 gene encodes a VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1309 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1309 precursor RNA is designated SEQ ID:1295, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1295 is located at position 28090 relative to the genome of Human Adenovirus D.

- [46274] VGAM1309 precursor RNA folds onto itself, forming VGAM1309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46275] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1309 folded precursor RNA into VGAM1309 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1309 RNA is designated SEQ ID:4020, and is provided hereinbelow with reference to the sequence listing part.

[46276] VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1309 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46277] VGAM1309 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1309 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1309 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[46278] The complementary binding of VGAM1309 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1309 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1309 host target RNA into VGAM1309 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46279] It is appreciated that VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1309 host target genes. The mRNA of

each one of this plurality of VGAM1309 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1309 RNA, herein designated VGAM RNA, and which when bound by VGAM1309 RNA causes inhibition of translation of respective one or more VGAM1309 host target proteins.

[46280] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1309 gene, herein designated VGAM GENE, on one or more VGAM1309 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[46281] It is yet further appreciated that a function of VGAM1309 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1309 correlate with, and may be deduced from, the identity of the host target genes which VGAM1309 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46282] Nucleotide sequences of the VGAM1309 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1309 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1309 are further described hereinbelow with reference to Table 1.

[46283] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1309 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1309 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46284] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1309 gene, herein designated VGAM is inhibition of expression of VGAM1309 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1309 correlate with, and may be deduced from, the identity of the target genes which VGAM1309 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46285] Cyclin-dependent Kinase Inhibitor 2D (p19, inhibits CDK4) (CDKN2D, Accession NM_001800) is a VGAM1309 host target gene. CDKN2D BINDING SITE1 and CDKN2D BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDKN2D, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2D BINDING SITE1 and CDKN2D BINDING SITE2, designated SEQ ID:7555 and SEQ ID:27817 respectively, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46286] A function of VGAM1309 is therefore inhibition of Cyclin-

dependent Kinase Inhibitor 2D (p19, inhibits CDK4) (CDKN2D, Accession NM_001800), a gene which interacts strongly with cdk4 and cdk6. Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2D. The function of CDKN2D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Nuclear RNA Export Factor 2 (NXF2, Accession NM_017809) is another VGAM1309 host target gene. NXF2 BINDING SITE1 and NXF2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NXF2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXF2 BINDING SITE1 and NXF2 BINDING SITE2, designated SEQ ID:19458 and SEQ ID:22590 respectively, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46287] Another function of VGAM1309 is therefore inhibition of Nuclear RNA Export Factor 2 (NXF2, Accession NM_017809), a gene which is involved in the export of

mrna from the nucleus to the cytoplasm. Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXF2. The function of NXF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. ZFP93 (Accession NM_004234) is another VGAM1309 host target gene. ZFP93 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP93, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP93 BINDING SITE, designated SEQ ID:10428, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46288] Another function of VGAM1309 is therefore inhibition of ZFP93 (Accession NM_004234). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP93. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033331) is another VGAM1309 host target gene. CDC14B BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:27161, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46289] Another function of VGAM1309 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033331). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. FLJ12806 (Accession NM_022831) is another VGAM1309 host target gene. FLJ12806 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12806 BINDING SITE, designated SEQ ID:23108, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46290] Another function of VGAM1309 is therefore inhibition of FLJ12806 (Accession NM_022831). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12806. HSPC065 (Accession NM_014157) is another VGAM1309 host target gene. HSPC065 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15454, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46291] Another function of VGAM1309 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. 5-hydroxytryptamine (serotonin) Receptor 3A (HTR3A, Accession NM_000869) is another VGAM1309 host target gene. HTR3A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTR3A, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR3A BINDING SITE, designated SEQ ID:6538, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46292] Another function of VGAM1309 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 3A (HTR3A, Accession NM_000869). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR3A. LANO (Accession NM_018214) is another VGAM1309 host target gene. LANO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LANO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANO BINDING SITE, designated SEQ ID:20129, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46293] Another function of VGAM1309 is therefore inhibition of LANO (Accession NM_018214). Accordingly, utilities of

VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANO. PAS Domain Containing Serine/threonine Kinase (PASK, Accession NM_015148) is another VGAM1309 host target gene. PASK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PASK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PASK BINDING SITE, designated SEQ ID:17503, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46294] Another function of VGAM1309 is therefore inhibition of PAS Domain Containing Serine/threonine Kinase (PASK, Accession NM_015148). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PASK. LOC145663 (Accession XM_096829) is another VGAM1309 host target gene. LOC145663 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC145663 BINDING SITE, designated SEQ ID:40551, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46295] Another function of VGAM1309 is therefore inhibition of LOC145663 (Accession XM_096829). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145663. LOC157507 (Accession XM_088312) is another VGAM1309 host target gene. LOC157507 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157507, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157507 BINDING SITE, designated SEQ ID:39606, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46296] Another function of VGAM1309 is therefore inhibition of LOC157507 (Accession XM_088312). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157507. LOC221337 (Accession XM_166387) is an-

other VGAM1309 host target gene. LOC221337 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221337 BINDING SITE, designated SEQ ID:44235, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46297] Another function of VGAM1309 is therefore inhibition of LOC221337 (Accession XM_166387). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221337. LOC92340 (Accession XM_044426) is another VGAM1309 host target gene. LOC92340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92340 BINDING SITE, designated SEQ ID:34200, to the nucleotide sequence of VGAM1309 RNA, herein designated VGAM RNA, also designated SEQ ID:4020.

[46298] Another function of VGAM1309 is therefore inhibition of LOC92340 (Accession XM_044426). Accordingly, utilities of VGAM1309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92340. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1310 (VGAM1310) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46299] VGAM1310 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1310 was detected is described hereinabove with reference to Figs. 1–8.

[46300] VGAM1310 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus D. VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46301] VGAM1310 gene encodes a VGAM1310 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1310 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1310 precursor RNA is designated SEQ ID:1296, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1296 is located at position 24460 relative to the genome of Human Adenovirus D.

[46302] VGAM1310 precursor RNA folds onto itself, forming VGAM1310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46303] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1310 folded precursor RNA into VGAM1310 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1310 RNA is designated SEQ ID:4021, and is provided hereinbelow with reference to the sequence listing part.

[46304] VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1310 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[46305] VGAM1310 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1310 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1310 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46306] The complementary binding of VGAM1310 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1310 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1310 host target RNA into VGAM1310 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46307] It is appreciated that VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1310 host target genes. The mRNA of each one of this plurality of VGAM1310 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1310 RNA, herein designated VGAM RNA, and which when bound by VGAM1310 RNA causes inhibition of translation of respective one or more VGAM1310 host target proteins.

[46308] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1310 gene, herein designated VGAM GENE, on one or more VGAM1310 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46309] It is yet further appreciated that a function of VGAM1310 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGAM1310 correlate with, and may be deduced from, the identity of the host target genes which VGAM1310 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46310] Nucleotide sequences of the VGAM1310 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1310 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1310 are further described hereinbelow with reference to Table 1.

[46311] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1310 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1310 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[46312] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1310 gene, herein designated VGAM is inhibition of expression of VGAM1310 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1310 correlate with, and may be deduced from, the identity of the target genes which VGAM1310 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46313] B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707) is a VGAM1310 host target gene. BCL7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7B BINDING SITE, designated SEQ ID:7437, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46314] A function of VGAM1310 is therefore inhibition of B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707), a gene which is of yet unknown function. Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with BCL7B. The function of BCL7B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM_019616) is another VGAM1310 host target gene. F7 BINDING SITE1 and F7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by F7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F7 BINDING SITE1 and F7 BINDING SITE2, designated SEQ ID:21239 and SEQ ID:5610 respectively, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46315] Another function of VGAM1310 is therefore inhibition of Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM_019616). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F7. RAD51-like 3 (*S. cerevisiae*) (RAD51L3, Accession NM_133630) is another VGAM1310 host target gene.

RAD51L3 BINDING SITE1 and RAD51L3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD51L3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD51L3 BINDING SITE1 and RAD51L3 BINDING SITE2, designated SEQ ID:28581 and SEQ ID:25181 respectively, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46316] Another function of VGAM1310 is therefore inhibition of RAD51-like 3 (*S. cerevisiae*) (RAD51L3, Accession NM_133630), a gene which may have a role in dna repair and recombination. Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD51L3. The function of RAD51L3 has been established by previous studies. The *S. cerevisiae* gene RAD51, which encodes a protein related to the ATP-binding *E. coli* RecA protein, is critical for DNA repair and meiotic recombination. Homologs of this gene have been identified in several species, including mouse and human. Pittman et al. (1998) reported the identification of a novel member of

the RAD51 gene family in both mouse and human. The mouse cDNA, Rad51d, isolated by screening EST databases with yeast RAD55 and human RAD51B amino acid sequences, encodes a predicted 329-amino acid protein with a molecular mass of 35,260 Da. Northern blot analysis revealed the presence of multiple transcripts of the Rad51d gene in all tissues examined. Southern analysis of genomic DNA from 7 mammalian species demonstrated that the RAD51D gene is conserved. Pittman et al. (1998) used the mouse nucleotide sequence to screen a human EST database and identified 2 RAD51D cDNA clones from human T-lymphocyte and placenta libraries; both cDNAs appeared to be variants of the mouse gene. The shorter cDNA represented an alternatively spliced product and excluded sequences corresponding to 2 exons in the mouse gene, one of which encodes the first ATP-binding motif. The longer cDNA skipped a single exon present in the mouse gene, resulting in a frameshift and a predicted truncated protein. The authors stated that if the frameshift is ignored, the full-length putative 289-amino acid protein shares 71% sequence identity with the predicted mouse protein, and the mouse and human RAD51D genes have 2 conserved ATP-binding do-

mains similar to other RecA-related genes. Cartwright et al. (1998) also isolated human and mouse RAD51L3, or R51H3, cDNAs. They found that the sequence of the predicted 328-amino acid human protein is 82% identical to that of mouse RAD51L3. Northern blot analysis revealed that human RAD51L3 is expressed as a 1.7-kb mRNA in all tissues, with the highest levels in testis.

[46317] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46318] Pittman, D. L.; Weinberg, L. R.; Schimenti, J. C. : Identification, characterization, and genetic mapping of Rad51d, a new mouse and human RAD51/RecA-related gene. *Genomics* 49: 103–111, 1998. ; and

[46319] Cartwright, R.; Dunn, A. M.; Simpson, P. J.; Tambini, C. E.; Thacker, J. : Isolation of novel human and mouse genes of the recA/RAD51 recombination-repair gene family. *Nucleic Acids Res.*

[46320] Further studies establishing the function and utilities of RAD51L3 are found in John Hopkins OMIM database record ID 602954, and in cited publications numbered 1597, 8639–160 and 8640 listed in the bibliography section hereinbelow, which are also hereby incorporated by

reference.DKFZp434G171 (Accession XM_086583) is another VGAM1310 host target gene. DKFZp434G171 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp434G171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434G171 BINDING SITE, designated SEQ ID:38777, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46321] Another function of VGAM1310 is therefore inhibition of DKFZp434G171 (Accession XM_086583). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434G171. FBP17 (Accession XM_052666) is another VGAM1310 host target gene. FBP17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36050, to the nucleotide se-

quence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46322] Another function of VGAM1310 is therefore inhibition of FBP17 (Accession XM_052666). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ00001 (Accession XM_088525) is another VGAM1310 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39785, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46323] Another function of VGAM1310 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ12056 (Accession NM_024933) is another VGAM1310 host target gene. FLJ12056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ12056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12056 BINDING SITE, designated SEQ ID:24470, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46324] Another function of VGAM1310 is therefore inhibition of FLJ12056 (Accession NM_024933). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12056. G Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM_014030) is another VGAM1310 host target gene. GIT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GIT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT1 BINDING SITE, designated SEQ ID:15257, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46325] Another function of VGAM1310 is therefore inhibition of G

Protein-coupled Receptor Kinase-interactor 1 (GIT1, Accession NM_014030). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT1. Mitogen-activated Protein Kinase 11 (MAPK11, Accession NM_002751) is another VGAM1310 host target gene. MAPK11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK11 BINDING SITE, designated SEQ ID:8628, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46326] Another function of VGAM1310 is therefore inhibition of Mitogen-activated Protein Kinase 11 (MAPK11, Accession NM_002751). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK11. Tumor Necrosis Factor Receptor Superfamily, Member 19-like (TNFRSF19L, Accession NM_032871) is another VGAM1310 host target gene. TNFRSF19L BINDING SITE is HOST TARGET binding

site found in the 5' untranslated region of mRNA encoded by TNFRSF19L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF19L BINDING SITE, designated SEQ ID:26687, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46327] Another function of VGAM1310 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 19-like (TNFRSF19L, Accession NM_032871). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF19L. LOC146475 (Accession XM_097006) is another VGAM1310 host target gene. LOC146475 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146475 BINDING SITE, designated SEQ ID:40701, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46328] Another function of VGAM1310 is therefore inhibition of LOC146475 (Accession XM_097006). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146475. LOC148753 (Accession XM_097515) is another VGAM1310 host target gene. LOC148753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148753 BINDING SITE, designated SEQ ID:40899, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46329] Another function of VGAM1310 is therefore inhibition of LOC148753 (Accession XM_097515). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148753. LOC220002 (Accession XM_166224) is another VGAM1310 host target gene. LOC220002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220002, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220002 BINDING SITE, designated SEQ ID:44050, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46330] Another function of VGAM1310 is therefore inhibition of LOC220002 (Accession XM_166224). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220002. LOC255265 (Accession XM_170902) is another VGAM1310 host target gene. LOC255265 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255265 BINDING SITE, designated SEQ ID:45659, to the nucleotide sequence of VGAM1310 RNA, herein designated VGAM RNA, also designated SEQ ID:4021.

[46331] Another function of VGAM1310 is therefore inhibition of LOC255265 (Accession XM_170902). Accordingly, utilities of VGAM1310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255265. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1311 (VGAM1311) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46332] VGAM1311 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1311 was detected is described hereinabove with reference to Figs. 1–8.

[46333] VGAM1311 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46334] VGAM1311 gene encodes a VGAM1311 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1311 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1311 precursor RNA is designated SEQ ID:1297, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1297 is located at position 3024 relative to the genome of Foot-and-mouth Disease Virus C.

- [46335] VGAM1311 precursor RNA folds onto itself, forming VGAM1311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46336] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1311 folded precursor RNA into VGAM1311 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1311 RNA is designated SEQ ID:4022, and is provided hereinbelow with reference to the sequence listing part.

[46337] VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1311 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46338] VGAM1311 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1311 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1311 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46339] The complementary binding of VGAM1311 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1311 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1311 host target RNA into VGAM1311 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46340] It is appreciated that VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1311 host target genes. The mRNA of each one of this plurality of VGAM1311 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1311 RNA, herein designated VGAM RNA, and which when bound by VGAM1311 RNA causes

inhibition of translation of respective one or more VGAM1311 host target proteins.

[46341] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1311 gene, herein designated VGAM GENE, on one or more VGAM1311 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46342] It is yet further appreciated that a function of VGAM1311 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1311 include diagnosis, prevention and

treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGAM1311 correlate with, and may be deduced from, the identity of the host target genes which VGAM1311 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46343] Nucleotide sequences of the VGAM1311 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1311 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1311 are further described hereinbelow with reference to Table 1.

[46344] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1311 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1311 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46345] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1311 gene, herein designated VGAM is inhibition of expression of VGAM1311 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1311 correlate with, and may be deduced from, the identity of the target genes which VGAM1311 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46346] Copine VII (CPNE7, Accession NM_014427) is a VGAM1311 host target gene. CPNE7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE7 BINDING SITE, designated SEQ ID:15786, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46347] A function of VGAM1311 is therefore inhibition of Copine VII (CPNE7, Accession NM_014427). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE7. Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM_054111) is another VGAM1311 host target gene. IHPK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IHPK3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IHPK3 BINDING SITE, designated SEQ ID:27655, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46348] Another function of VGAM1311 is therefore inhibition of Inositol Hexaphosphate Kinase 3 (IHPK3, Accession NM_054111). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IHPK3. Kruppel-like Factor 8 (KLF8, Accession NM_007250) is another VGAM1311 host target gene. KLF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLF8 BINDING SITE, designated SEQ ID:14121, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46349] Another function of VGAM1311 is therefore inhibition of Kruppel-like Factor 8 (KLF8, Accession NM_007250). Ac-

cordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLF8. Matrix Metalloproteinase 19 (MMP19, Accession NM_022790) is another VGAM1311 host target gene. MMP19 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MMP19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE, designated SEQ ID:23073, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46350] Another function of VGAM1311 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_022790). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. Transcription Factor 20 (AR1) (TCF20, Accession XM_040067) is another VGAM1311 host target gene. TCF20 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TCF20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF20 BINDING SITE, designated SEQ ID:33247, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46351] Another function of VGAM1311 is therefore inhibition of Transcription Factor 20 (AR1) (TCF20, Accession XM_040067), a gene which is strongly similar to murine Tcf20 and may act as a transcription activator. Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF20. The function of TCF20 has been established by previous studies. Stromelysins, which are the metalloproteinases with the widest substrate specificities, play a critical role in tumor invasion and metastasis. See 185261. Stromelysin expression is induced by mitogens, oncogenes, and inflammatory cytokines. A 19-nucleotide promoter element called the SPRE (stromelysin-1 PDGF-responsive element), controls stromelysin-1 (OMIM Ref. No. 185250) expression in response to mitogen stimulation. Sanz et al. (1995) screened a mouse fibroblast expression library to identify factors that bind to the SPRE. They isolated a cDNA encoding a predicted 937-amino

acid protein designated SPBP for 'SPRE-binding protein.' SPBP contains several features characteristic of transcription factors, including a putative leucine zipper region, a nuclear localization signal, and a basic domain similar to the DNA-binding domain found in the Fos (OMIM Ref. No. 164810)–Jun (OMIM Ref. No. 165160) family of transcription factors. However, while in Fos and Jun the ZIP and DNA-binding domains lie very close together, in SPBP they are widely separated. Sanz et al. (1995) found that expression of SPBP in mammalian cells activated transcription of a reporter gene construct containing either the full-length stromelysin promoter or a single copy of the SPRE inserted upstream of a heterologous promoter. Rajadhyaksha et al. (1998) identified cDNAs encoding AR1, a human SPBP homolog. By analysis of somatic cell hybrids and by fluorescence in situ hybridization, Rajadhyaksha et al. (1998) localized the AR1 gene to 22q13.3.

[46352] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46353] Rajadhyaksha, A. Riviere, M.; Van Vooren, P.; Szpirer, J.; Szpirer, C.; Babin, J.; Bina, M. : Assignment of AR1, transcription factor 20 (TCF20), to human chromosome

22q13.3 with somatic cell hybrids and in situ hybridization. Cytogenet. Cell Genet. 81: 176–177, 1998. ; and

[46354] Sanz, L.; Moscat, J.; Diaz-Meco, M. T. : Molecular characterization of a novel transcription factor that controls stromelysin expression. Molec. Cell. Biol. 15: 3164–3170, 1995.

[46355] Further studies establishing the function and utilities of TCF20 are found in John Hopkins OMIM database record ID 603107, and in cited publications numbered 8494–8495 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. STAF42 (Accession NM_053053) is another VGAM1311 host target gene. STAF42 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STAF42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAF42 BINDING SITE, designated SEQ ID:27596, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46356] Another function of VGAM1311 is therefore inhibition of STAF42 (Accession NM_053053). Accordingly, utilities of

VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAF42. LOC146520 (Accession XM_085492) is another VGAM1311 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38185, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46357] Another function of VGAM1311 is therefore inhibition of LOC146520 (Accession XM_085492). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC253502 (Accession XM_170561) is another VGAM1311 host target gene. LOC253502 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC253502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC253502 BINDING SITE, designated SEQ ID:45379, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46358] Another function of VGAM1311 is therefore inhibition of LOC253502 (Accession XM_170561). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253502. LOC90750 (Accession XM_033868) is another VGAM1311 host target gene. LOC90750 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90750, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90750 BINDING SITE, designated SEQ ID:31973, to the nucleotide sequence of VGAM1311 RNA, herein designated VGAM RNA, also designated SEQ ID:4022.

[46359] Another function of VGAM1311 is therefore inhibition of LOC90750 (Accession XM_033868). Accordingly, utilities of VGAM1311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90750. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1312 (VGAM1312) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46360] VGAM1312 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1312 was detected is described hereinabove with reference to Figs. 1–8.

[46361] VGAM1312 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46362] VGAM1312 gene encodes a VGAM1312 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1312 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1312 precursor RNA is designated SEQ ID:1298, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1298 is located at position 1074 relative to the

genome of Foot-and-mouth Disease Virus C.

[46363] VGAM1312 precursor RNA folds onto itself, forming VGAM1312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46364] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1312 folded precursor RNA into VGAM1312 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1312 RNA is designated SEQ ID:4023, and is provided hereinbelow with reference to the sequence listing part.

[46365] VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1312 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46366] VGAM1312 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1312 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1312 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[46367] The complementary binding of VGAM1312 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1312 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1312 host target RNA into VGAM1312 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46368] It is appreciated that VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1312 host target genes. The mRNA of each one of this plurality of VGAM1312 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1312 RNA, herein designated VGAM RNA, and which when bound by VGAM1312 RNA causes inhibition of translation of respective one or more VGAM1312 host target proteins.

[46369] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1312 gene, herein designated VGAM GENE, on one or more VGAM1312 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46370] It is yet further appreciated that a function of VGAM1312 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of

VGAM1312 correlate with, and may be deduced from, the identity of the host target genes which VGAM1312 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46371] Nucleotide sequences of the VGAM1312 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1312 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1312 are further described hereinbelow with reference to Table 1.

[46372] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1312 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1312 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46373] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1312 gene, herein designated VGAM is inhibition of expression of VGAM1312 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1312 correlate with, and may be deduced

from, the identity of the target genes which VGAM1312 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46374] Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823) is a VGAM1312 host target gene. PKIA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PKIA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIA BINDING SITE, designated SEQ ID:13700, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46375] A function of VGAM1312 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIA. Solute Carrier Family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), Member 1 (SLC1A1, Accession NM_004170) is another VGAM1312 host target gene. SLC1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SLC1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A1 BINDING SITE, designated SEQ ID:10379, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46376] Another function of VGAM1312 is therefore inhibition of Solute Carrier Family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), Member 1 (SLC1A1, Accession NM_004170), a gene which is a glutamate transporter, essential for terminating the postsynaptic action of glutamate by rapidly removing it from the synaptic cleft. Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A1. The function of SLC1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Solute Carrier Family 6 (neurotransmitter transporter, betaine/GABA), Member 12 (SLC6A12, Accession NM_003044) is another VGAM1312 host target gene. SLC6A12 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by SLC6A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A12 BINDING SITE, designated SEQ ID:9009, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46377] Another function of VGAM1312 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, betaine/GABA), Member 12 (SLC6A12, Accession NM_003044), a gene which transports betaine and gaba. Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A12. The function of SLC6A12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM293. Transporter 2, ATP-binding Cassette, Subfamily B (MDR/TAP) (TAP2, Accession NM_000544) is another VGAM1312 host target gene. TAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAP2 BINDING SITE, designated SEQ ID:6141, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46378] Another function of VGAM1312 is therefore inhibition of Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544), a gene which is involved in the transport of antigens from the cytoplasm to a membrane-bound compartment for association with mhc class i molecules. Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAP2. The function of TAP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Chromosome 20 Open Reading Frame 4 (C20orf4, Accession NM_015511) is another VGAM1312 host target gene. C20orf4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of C20orf4 BINDING SITE, designated SEQ ID:17771, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46379] Another function of VGAM1312 is therefore inhibition of Chromosome 20 Open Reading Frame 4 (C20orf4, Accession NM_015511). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf4. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769) is another VGAM1312 host target gene. CHST4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST4 BINDING SITE, designated SEQ ID:12335, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46380] Another function of VGAM1312 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769). Accordingly, utilities of

VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST4. CTAGE-1 (Accession NM_022663) is another VGAM1312 host target gene. CTAGE-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTAGE-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTAGE-1 BINDING SITE, designated SEQ ID:22909, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46381] Another function of VGAM1312 is therefore inhibition of CTAGE-1 (Accession NM_022663). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTAGE-1. HSPC129 (Accession NM_016396) is another VGAM1312 host target gene. HSPC129 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC129

BINDING SITE, designated SEQ ID:18534, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46382] Another function of VGAM1312 is therefore inhibition of HSPC129 (Accession NM_016396). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC129. KIAA1323 (Accession XM_032146) is another VGAM1312 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31569, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46383] Another function of VGAM1312 is therefore inhibition of KIAA1323 (Accession XM_032146). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. KIAA1462 (Accession XM_166132) is another VGAM1312 host target gene. KIAA1462 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43920, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46384] Another function of VGAM1312 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. P66 (Accession NM_020699) is another VGAM1312 host target gene. P66 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by P66, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P66 BINDING SITE, designated SEQ ID:21848, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46385] Another function of VGAM1312 is therefore inhibition of

P66 (Accession NM_020699). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P66. PRO1635 (Accession NM_018589) is another VGAM1312 host target gene. PRO1635 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1635 BINDING SITE, designated SEQ ID:20667, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46386] Another function of VGAM1312 is therefore inhibition of PRO1635 (Accession NM_018589). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1635. TRIP-Br2 (Accession NM_014755) is another VGAM1312 host target gene. TRIP-Br2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIP-Br2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16479, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46387] Another function of VGAM1312 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. LOC221178 (Accession XM_167936) is another VGAM1312 host target gene. LOC221178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221178 BINDING SITE, designated SEQ ID:44926, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46388] Another function of VGAM1312 is therefore inhibition of LOC221178 (Accession XM_167936). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221178. LOC221300 (Accession XM_166322) is an-

other VGAM1312 host target gene. LOC221300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221300 BINDING SITE, designated SEQ ID:44148, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46389] Another function of VGAM1312 is therefore inhibition of LOC221300 (Accession XM_166322). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221300. LOC221712 (Accession XM_168059) is another VGAM1312 host target gene. LOC221712 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221712 BINDING SITE, designated SEQ ID:44975, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46390] Another function of VGAM1312 is therefore inhibition of LOC221712 (Accession XM_168059). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221712. LOC256849 (Accession XM_173059) is another VGAM1312 host target gene. LOC256849 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256849, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256849 BINDING SITE, designated SEQ ID:46313, to the nucleotide sequence of VGAM1312 RNA, herein designated VGAM RNA, also designated SEQ ID:4023.

[46391] Another function of VGAM1312 is therefore inhibition of LOC256849 (Accession XM_173059). Accordingly, utilities of VGAM1312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256849. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1313 (VGAM1313) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[46392] VGAM1313 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1313 was detected is described hereinabove with reference to Figs. 1–8.

[46393] VGAM1313 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46394] VGAM1313 gene encodes a VGAM1313 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1313 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1313 precursor RNA is designated SEQ ID:1299, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1299 is located at position 4912 relative to the genome of Foot-and-mouth Disease Virus C.

[46395] VGAM1313 precursor RNA folds onto itself, forming VGAM1313 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46396] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1313 folded precursor RNA into VGAM1313 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1313 RNA is designated SEQ ID:4024, and is provided hereinbelow with reference to the sequence listing part.

[46397] VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1313 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46398] VGAM1313 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1313 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1313 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46399] The complementary binding of VGAM1313 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1313 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1313 host target RNA into VGAM1313 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46400] It is appreciated that VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1313 host target genes. The mRNA of each one of this plurality of VGAM1313 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1313 RNA, herein designated VGAM RNA, and which when bound by VGAM1313 RNA causes inhibition of translation of respective one or more VGAM1313 host target proteins.

[46401] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1313 gene, herein designated VGAM GENE, on one or more VGAM1313 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46402] It is yet further appreciated that a function of VGAM1313 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGAM1313 correlate with, and may be deduced from, the identity of the host target genes which VGAM1313 binds and inhibits, and the function of these host target genes,

as elaborated hereinbelow.

[46403] Nucleotide sequences of the VGAM1313 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1313 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1313 are further described hereinbelow with reference to Table 1.

[46404] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1313 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1313 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46405] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1313 gene, herein designated VGAM is inhibition of expression of VGAM1313 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1313 correlate with, and may be deduced from, the identity of the target genes which VGAM1313 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46406] Aquaporin 6, Kidney Specific (AQP6, Accession NM_001652) is a VGAM1313 host target gene. AQP6 BINDING SITE1 and AQP6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AQP6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP6 BINDING SITE1 and AQP6 BINDING SITE2, designated SEQ ID:7359 and SEQ ID:27614 respectively, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46407] A function of VGAM1313 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM_001652), a gene which participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340.GRB2-associated Binding Protein 2 (GAB2, Ac-

cession NM_012296) is another VGAM1313 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:14652 and SEQ ID:27847 respectively, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46408] Another function of VGAM1313 is therefore inhibition of GRB2-associated Binding Protein 2 (GAB2, Accession NM_012296), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53.HMT1 HnRNP Methyltransferase-like 1 (*S. cerevisiae*) (HRMT1L1, Accession XM_036869) is another VGAM1313 host target gene. HRMT1L1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRMT1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRMT1L1 BINDING SITE, designated SEQ ID:32506, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46409] Another function of VGAM1313 is therefore inhibition of HMT1 HnRNP Methyltransferase-like 1 (*S. cerevisiae*) (HRMT1L1, Accession XM_036869), a gene which is post-translational methylation of arginine residues. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRMT1L1. The function of HRMT1L1 has been established by previous studies. Katsanis et al. (1997) isolated a novel transcript from chromosome 21 that they found to be similar to the rat protein arginine N-methyltransferase-1 gene (PRMT1) reported by Lin et al. (1996). Katsanis et al. (1997) mapped the human gene (HRMT1L1) to chromosome 21 by study of monochromosomal cell hybrids and fine mapped the gene by PCR analysis of a partial chromosome 21 hybrid panel to a telom-

eric position on 21q22.3. Hybridization to a YAC that was positive for S100B (OMIM Ref. No. 176990) indicated that HRMT1L1 is no more than 10 kb from S100B. S100B was the most telomeric chromosome 21 gene known at that time. Katsanis et al. (1997) found that HRMT1L1 was expressed in all tissues they investigated. They noted that the function of such protein methyltransferases is post-translational methylation of arginine residues. Two types of activity had been described, attributed to different classes of enzymes. One methylates myelin protein zero (MPZ; 159440); the other was originally thought to methylate histones, but was later found to methylate hnRNPs far more efficiently. The authors suggested that this human homolog of yeast RMT1 associates with hnRNPs. Scott et al. (1998) further characterized HRMT1L1 and HRMT1L2. By Northern blot analysis, they found that HRMT1L1 is expressed as a 2.4-kb transcript in various adult and fetal tissues. The HRMT1L1 protein could not methylate hnRNPA1 (OMIM Ref. No. 164017) or any other tested substrate in vitro, and did not complement a yeast arginine methyltransferase mutant strain.

[46410] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [46411] Lin, W. J.; Gary, J. D.; Yang, M. C.; Clarke, S.; Herschman, H. R. : The mammalian intermediate–early TIS21 protein and the leukemia–associated BTG1 protein interact with a protein–arginine N–methyltransferase. J. Biol. Chem. 271: 15034–15044, 1996. ; and
- [46412] Scott, H. S.; Antonarakis, S. E.; Lalioti, M. D.; Rossier, C.; Silver, P. A.; Henry, M. F. : Identification and characterization of two putative human arginine methyltransferases (HRMT1.
- [46413] Further studies establishing the function and utilities of HRMT1L1 are found in John Hopkins OMIM database record ID 601961, and in cited publications numbered 5819–5821 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leucine Zipper–EF–hand Containing Transmembrane Protein 1 (LETM1, Accession NM_012318) is another VGAM1313 host target gene. LETM1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LETM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LETM1 BINDING SITE, des–

ignated SEQ ID:14697, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46414] Another function of VGAM1313 is therefore inhibition of Leucine Zipper-EF-hand Containing Transmembrane Protein 1 (LETM1, Accession NM_012318). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LETM1. Microtubule-associated Protein, RP/EB Family, Member 1 (MAPRE1, Accession NM_012325) is another VGAM1313 host target gene. MAPRE1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE1 BINDING SITE, designated SEQ ID:14708, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46415] Another function of VGAM1313 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 1 (MAPRE1, Accession NM_012325). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MAPRE1. Myotubularin Related Protein 6 (MTMR6, Accession XM_167970) is another VGAM1313 host target gene. MTMR6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MTMR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR6 BINDING SITE, designated SEQ ID:44936, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46416] Another function of VGAM1313 is therefore inhibition of Myotubularin Related Protein 6 (MTMR6, Accession XM_167970). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR6. Natural Killer-tumor Recognition Sequence (NKTR, Accession NM_005385) is another VGAM1313 host target gene. NKTR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NKTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates

the complementarity of the nucleotide sequences of NKTR BINDING SITE, designated SEQ ID:11863, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46417] Another function of VGAM1313 is therefore inhibition of Natural Killer–tumor Recognition Sequence (NKTR, Accession NM_005385), a gene which is involved in the function of nk cells. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKTR. The function of NKTR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM133.Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM1313 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28444, SEQ ID:28461 and SEQ

ID:17180 respectively, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46418] Another function of VGAM1313 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM_014787) is another VGAM1313 host target gene. DNAJC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC6 BINDING SITE, designated SEQ ID:16660, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46419] Another function of VGAM1313 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM_014787). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC6. FLJ10314 (Accession NM_018055) is another VGAM1313 host target gene. FLJ10314 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10314, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10314 BINDING SITE, designated SEQ ID:19817, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46420] Another function of VGAM1313 is therefore inhibition of FLJ10314 (Accession NM_018055). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10314. FLJ20171 (Accession NM_017697) is another VGAM1313 host target gene. FLJ20171 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20171, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20171 BINDING SITE, designated SEQ ID:19261, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46421] Another function of VGAM1313 is therefore inhibition of FLJ20171 (Accession NM_017697). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20171. KIAA0229 (Accession XM_166478) is another VGAM1313 host target gene. KIAA0229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0229 BINDING SITE, designated SEQ ID:44403, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46422] Another function of VGAM1313 is therefore inhibition of KIAA0229 (Accession XM_166478). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0229. KIAA0410 (Accession NM_014778) is another VGAM1313 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16619, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46423] Another function of VGAM1313 is therefore inhibition of KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0410. KIAA0565 (Accession XM_039912) is another VGAM1313 host target gene. KIAA0565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0565 BINDING SITE, designated SEQ ID:33215, to the

nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46424] Another function of VGAM1313 is therefore inhibition of KIAA0565 (Accession XM_039912). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0565. KIAA1462 (Accession XM_166132) is another VGAM1313 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43918, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46425] Another function of VGAM1313 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. MIC2 Like 1 (MIC2L1, Accession NM_031462) is another VGAM1313 host target gene. MIC2L1 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by MIC2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIC2L1 BINDING SITE, designated SEQ ID:25490, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46426] Another function of VGAM1313 is therefore inhibition of MIC2 Like 1 (MIC2L1, Accession NM_031462). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIC2L1. Nuclear Autoantigenic Sperm Protein (histone-binding) (NASP, Accession XM_042664) is another VGAM1313 host target gene. NASP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NASP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NASP BINDING SITE, designated SEQ ID:33738, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46427] Another function of VGAM1313 is therefore inhibition of

Nuclear Autoantigenic Sperm Protein (histone-binding) (NASP, Accession XM_042664). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NASP. ZFP106 (Accession NM_022473) is another VGAM1313 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22830, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46428] Another function of VGAM1313 is therefore inhibition of ZFP106 (Accession NM_022473). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC152220 (Accession XM_098176) is another VGAM1313 host target gene. LOC152220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152220, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152220 BINDING SITE, designated SEQ ID:41443, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46429] Another function of VGAM1313 is therefore inhibition of LOC152220 (Accession XM_098176). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152220. LOC254057 (Accession XM_173085) is another VGAM1313 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254057 BINDING SITE, designated SEQ ID:46349, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46430] Another function of VGAM1313 is therefore inhibition of LOC254057 (Accession XM_173085). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC254057. LOC254302 (Accession XM_171219) is another VGAM1313 host target gene. LOC254302 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254302 BINDING SITE, designated SEQ ID:46005, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46431] Another function of VGAM1313 is therefore inhibition of LOC254302 (Accession XM_171219). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254302. LOC254874 (Accession XM_171217) is another VGAM1313 host target gene. LOC254874 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254874, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254874 BINDING SITE, designated SEQ ID:46004, to the nucleotide sequence of VGAM1313 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4024.

[46432] Another function of VGAM1313 is therefore inhibition of LOC254874 (Accession XM_171217). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254874. LOC256207 (Accession XM_170837) is another VGAM1313 host target gene. LOC256207 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256207, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256207 BINDING SITE, designated SEQ ID:45616, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46433] Another function of VGAM1313 is therefore inhibition of LOC256207 (Accession XM_170837). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256207. LOC257407 (Accession XM_173078) is another VGAM1313 host target gene. LOC257407 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257407, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257407 BINDING SITE, designated SEQ ID:46335, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46434] Another function of VGAM1313 is therefore inhibition of LOC257407 (Accession XM_173078). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257407. LOC90170 (Accession XM_029589) is another VGAM1313 host target gene. LOC90170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90170 BINDING SITE, designated SEQ ID:30908, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46435] Another function of VGAM1313 is therefore inhibition of LOC90170 (Accession XM_029589). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC90170. LOC90268 (Accession XM_030424) is another VGAM1313 host target gene. LOC90268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90268 BINDING SITE, designated SEQ ID:31043, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46436] Another function of VGAM1313 is therefore inhibition of LOC90268 (Accession XM_030424). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90268. LOC91496 (Accession XM_038788) is another VGAM1313 host target gene. LOC91496 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91496 BINDING SITE, designated SEQ ID:32917, to the

nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46437] Another function of VGAM1313 is therefore inhibition of LOC91496 (Accession XM_038788). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91496. LOC91661 (Accession NM_138372) is another VGAM1313 host target gene. LOC91661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91661 BINDING SITE, designated SEQ ID:28752, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46438] Another function of VGAM1313 is therefore inhibition of LOC91661 (Accession NM_138372). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91661. LOC92997 (Accession XM_048690) is another VGAM1313 host target gene. LOC92997 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC92997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92997 BINDING SITE, designated SEQ ID:35220, to the nucleotide sequence of VGAM1313 RNA, herein designated VGAM RNA, also designated SEQ ID:4024.

[46439] Another function of VGAM1313 is therefore inhibition of LOC92997 (Accession XM_048690). Accordingly, utilities of VGAM1313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92997. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1314 (VGAM1314) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46440] VGAM1314 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1314 was detected is described hereinabove with reference to Figs. 1-8.

[46441] VGAM1314 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46442] VGAM1314 gene encodes a VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1314 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1314 precursor RNA is designated SEQ ID:1300, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1300 is located at position 4399 relative to the genome of Foot-and-mouth Disease Virus C.

[46443] VGAM1314 precursor RNA folds onto itself, forming VGAM1314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46444] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1314 folded precursor RNA into VGAM1314 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1314 RNA is designated SEQ ID:4025, and is provided hereinbelow with reference to the sequence listing part.

[46445] VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1314 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46446] VGAM1314 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1314 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1314 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46447] The complementary binding of VGAM1314 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1314 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1314

host target RNA into VGAM1314 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46448] It is appreciated that VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1314 host target genes. The mRNA of each one of this plurality of VGAM1314 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1314 RNA, herein designated VGAM RNA, and which when bound by VGAM1314 RNA causes inhibition of translation of respective one or more VGAM1314 host target proteins.

[46449] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1314 gene, herein designated VGAM GENE, on one or more VGAM1314 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46450] It is yet further appreciated that a function of VGAM1314 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGAM1314 correlate with, and may be deduced from, the identity of the host target genes which VGAM1314 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46451] Nucleotide sequences of the VGAM1314 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1314 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1314 are further

described hereinbelow with reference to Table 1.

[46452] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1314 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1314 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46453] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1314 gene, herein designated VGAM is inhibition of expression of VGAM1314 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1314 correlate with, and may be deduced from, the identity of the target genes which VGAM1314 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46454] BCL2-like 2 (BCL2L2, Accession NM_004050) is a VGAM1314 host target gene. BCL2L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BCL2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L2 BIND-

ING SITE, designated SEQ ID:10257, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46455] A function of VGAM1314 is therefore inhibition of BCL2-like 2 (BCL2L2, Accession NM_004050), a gene which promotes cell survival. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L2. The function of BCL2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM431. Caspase Recruitment Domain Family, Member 15 (CARD15, Accession NM_022162) is another VGAM1314 host target gene. CARD15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD15 BINDING SITE, designated SEQ ID:22716, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46456] Another function of VGAM1314 is therefore inhibition of

Caspase Recruitment Domain Family, Member 15

(CARD15, Accession NM_022162), a gene which serves as an intracellular receptor for bacterial products in monocytes and transduces signals leading to NF κ B activation. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD15. The function of CARD15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM126.Diaphorase (NADH) (cytochrome b-5 reductase) (DIA1, Accession NM_007326) is another VGAM1314 host target gene. DIA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIA1 BINDING SITE, designated SEQ ID:14247, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46457] Another function of VGAM1314 is therefore inhibition of Diaphorase (NADH) (cytochrome b-5 reductase) (DIA1,

Accession NM_007326). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIA1. Fibroblast Growth Factor 7 (keratinocyte growth factor) (FGF7, Accession NM_002009) is another VGAM1314 host target gene. FGF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF7 BINDING SITE, designated SEQ ID:7750, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46458] Another function of VGAM1314 is therefore inhibition of Fibroblast Growth Factor 7 (keratinocyte growth factor) (FGF7, Accession NM_002009), a gene which growth factor active on keratinocytes. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF7. The function of FGF7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM678. Glycoprotein A Repetitions Predominant

(GARP, Accession NM_005512) is another VGAM1314 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12030, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46459] Another function of VGAM1314 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARP. Glucosaminyl (N-acetyl) Transferase 2, I-branching Enzyme (GCNT2, Accession NM_001491) is another VGAM1314 host target gene. GCNT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GCNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCNT2 BINDING SITE, designated SEQ

ID:7238, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46460] Another function of VGAM1314 is therefore inhibition of Glucosaminyl (N-acetyl) Transferase 2, I-branching Enzyme (GCNT2, Accession NM_001491), a gene which converts linear into branched poly-n-acetyllactosaminoglycans. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCNT2. The function of GCNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM943. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_138619) is another VGAM1314 host target gene. GGA3 BINDING SITE1 and GGA3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA3 BINDING SITE1 and GGA3 BINDING SITE2, designated SEQ ID:28903 and SEQ

ID:15200 respectively, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46461] Another function of VGAM1314 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 3 (GGA3, Accession NM_138619), a gene which may play a role in the regulation of membrane traffic through the trans-golgi network. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA3. The function of GGA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM353. Nuclear Respiratory Factor 1 (NRF1, Accession XM_011548) is another VGAM1314 host target gene. NRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRF1 BINDING SITE, designated SEQ ID:30191, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46462] Another function of VGAM1314 is therefore inhibition of Nuclear Respiratory Factor 1 (NRF1, Accession XM_011548), a gene which is a basic leucine zipper (bZIP) transcriptional activator and involved in the regulation of genes for EIF2A and respiratory subunits. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRF1. The function of NRF1 has been established by previous studies. Gopalakrishnan and Scarpulla (1995) noted that the electron transport chain and oxidative phosphorylation system rely on the functional interplay of gene products expressed from both nuclear and mitochondrial genomes. Because of the limited coding capacity of the mitochondrial chromosome, nuclear genes must provide most of the respiratory subunits and all of the gene products necessary for mitochondrial DNA transcription and replication. Nuclear respiratory factor-1 (NRF1) is a transcription factor that acts on nuclear genes encoding respiratory subunits and components of the mitochondrial transcription and replication machinery. Virbasius et al. (1993) cloned the human NRF1 cDNA from HeLa cells using degenerate primers based on partial tryptic peptide sequences and showed a predicted 504 amino acid pro-

tein encoded by a 2,970 nucleotide cDNA. The recombinantly expressed protein activated transcription of several NRF1-responsive promoters. Animal model experiments lend further support to the function of NRF1.

[46463] It is appreciated that the abovementioned animal model for NRF1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[46464] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46465] Gopalakrishnan, L.; Scarpulla, R. C. : Structure, expression, and chromosomal assignment of the human gene encoding nuclear respiratory factor 1. J. Biol. Chem. 270: 18019–18025, 1995. ; and

[46466] Virbasius, C. A.; Virbasius, J. V.; Scarpulla, R. C. : NRF-1, an activator involved in nuclear-mitochondrial interactions, utilizes a new DNA-binding domain conserved in a family of dev.

[46467] Further studies establishing the function and utilities of NRF1 are found in John Hopkins OMIM database record ID 600879, and in cited publications numbered 6852–6855, 714 and 10060 listed in the bibliography section herein–

below, which are also hereby incorporated by reference. Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531) is another VGAM1314 host target gene. NTSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTSR1 BINDING SITE, designated SEQ ID:8368, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46468] Another function of VGAM1314 is therefore inhibition of Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531), a gene which is associated with g proteins that activate a phosphatidylinositol- calcium second messenger system. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTSR1. The function of NTSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Synaptogyrin 1 (SYNGR1, Accession

NM_004711) is another VGAM1314 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE, designated SEQ ID:11065, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46469] Another function of VGAM1314 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Transcription Factor 1, Hepatic; LF-B1, Hepatic Nuclear Factor (HNF1), Albumin Proximal Factor (TCF1, Accession NM_000545) is another VGAM1314 host target gene. TCF1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF1 BINDING SITE, designated SEQ ID:6148, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46470] Another function of VGAM1314 is therefore inhibition of Transcription Factor 1, Hepatic; LF-B1, Hepatic Nuclear Factor (HNF1), Albumin Proximal Factor (TCF1, Accession NM_000545), a gene which is required for the expression of several liver specific genes. binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF1. The function of TCF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Aquaporin 9 (AQP9, Accession NM_020980) is another VGAM1314 host target gene. AQP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP9, correspond-

ing to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP9 BINDING SITE, designated SEQ ID:21968, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46471] Another function of VGAM1314 is therefore inhibition of Aquaporin 9 (AQP9, Accession NM_020980). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP9. Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175) is another VGAM1314 host target gene. C8orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf2 BINDING SITE, designated SEQ ID:14022, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46472] Another function of VGAM1314 is therefore inhibition of Chromosome 8 Open Reading Frame 2 (C8orf2, Accession

NM_007175). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf2. DKFZP586I2223 (Accession NM_015438) is another VGAM1314 host target gene. DKFZP586I2223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586I2223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586I2223 BINDING SITE, designated SEQ ID:17731, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46473] Another function of VGAM1314 is therefore inhibition of DKFZP586I2223 (Accession NM_015438). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586I2223. FLJ20275 (Accession NM_017737) is another VGAM1314 host target gene. FLJ20275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ20275 BINDING SITE, designated SEQ ID:19322, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46474] Another function of VGAM1314 is therefore inhibition of FLJ20275 (Accession NM_017737). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20275. FLJ21742 (Accession NM_032207) is another VGAM1314 host target gene. FLJ21742 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21742 BINDING SITE, designated SEQ ID:25913, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46475] Another function of VGAM1314 is therefore inhibition of FLJ21742 (Accession NM_032207). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21742. FYVE and Coiled-coil Domain Containing 1

(FYCO1, Accession NM_024513) is another VGAM1314 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23709, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46476] Another function of VGAM1314 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Hypermethylated In Cancer 2 (HIC2, Accession XM_036937) is another VGAM1314 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32529, to the nucleotide se-

quence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46477] Another function of VGAM1314 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM_036937). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. KIAA0319 (Accession NM_014809) is another VGAM1314 host target gene. KIAA0319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0319 BINDING SITE, designated SEQ ID:16762, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46478] Another function of VGAM1314 is therefore inhibition of KIAA0319 (Accession NM_014809). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0319. KIAA0672 (Accession NM_014859) is another VGAM1314 host target gene. KIAA0672 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0672, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0672 BINDING SITE, designated SEQ ID:16919, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46479] Another function of VGAM1314 is therefore inhibition of KIAA0672 (Accession NM_014859). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0672. KIAA1036 (Accession NM_014909) is another VGAM1314 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17133, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46480] Another function of VGAM1314 is therefore inhibition of

KIAA1036 (Accession NM_014909). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. KIAA1280 (Accession XM_045766) is another VGAM1314 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34551, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46481] Another function of VGAM1314 is therefore inhibition of KIAA1280 (Accession XM_045766). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. KIAA1855 (Accession XM_166453) is another VGAM1314 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44358, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46482] Another function of VGAM1314 is therefore inhibition of KIAA1855 (Accession XM_166453). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211) is another VGAM1314 host target gene. LOXL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOXL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL4 BINDING SITE, designated SEQ ID:25930, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46483] Another function of VGAM1314 is therefore inhibition of Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with LOXL4. SCMH1 (Accession NM_012236) is another VGAM1314 host target gene. SCMH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCMH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCMH1 BINDING SITE, designated SEQ ID:14539, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46484] Another function of VGAM1314 is therefore inhibition of SCMH1 (Accession NM_012236). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCMH1. Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM_004782) is another VGAM1314 host target gene. SNAP29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP29 BINDING SITE, designated SEQ ID:11187, to the nucleotide sequence of VGAM1314 RNA,

herein designated VGAM RNA, also designated SEQ ID:4025.

[46485] Another function of VGAM1314 is therefore inhibition of Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM_004782). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP29. LOC112868 (Accession XM_053402) is another VGAM1314 host target gene. LOC112868 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC112868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112868 BINDING SITE, designated SEQ ID:36084, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46486] Another function of VGAM1314 is therefore inhibition of LOC112868 (Accession XM_053402). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112868. LOC132880 (Accession XM_059609) is another VGAM1314 host target gene. LOC132880 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC132880, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132880 BINDING SITE, designated SEQ ID:37031, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46487] Another function of VGAM1314 is therefore inhibition of LOC132880 (Accession XM_059609). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132880. LOC136015 (Accession XM_072440) is another VGAM1314 host target gene. LOC136015 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC136015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC136015 BINDING SITE, designated SEQ ID:37501, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46488] Another function of VGAM1314 is therefore inhibition of

LOC136015 (Accession XM_072440). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC136015. LOC142927 (Accession XM_084380) is another VGAM1314 host target gene. LOC142927 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC142927, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142927 BINDING SITE, designated SEQ ID:37567, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46489] Another function of VGAM1314 is therefore inhibition of LOC142927 (Accession XM_084380). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142927. LOC143425 (Accession XM_113695) is another VGAM1314 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC143425 BINDING SITE, designated SEQ ID:42355, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46490] Another function of VGAM1314 is therefore inhibition of LOC143425 (Accession XM_113695). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC145566 (Accession XM_085174) is another VGAM1314 host target gene. LOC145566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145566 BINDING SITE, designated SEQ ID:37897, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46491] Another function of VGAM1314 is therefore inhibition of LOC145566 (Accession XM_085174). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145566. LOC151391 (Accession XM_098050) is an-

other VGAM1314 host target gene. LOC151391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151391 BINDING SITE, designated SEQ ID:41335, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46492] Another function of VGAM1314 is therefore inhibition of LOC151391 (Accession XM_098050). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151391. LOC152200 (Accession XM_098174) is another VGAM1314 host target gene. LOC152200 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152200, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152200 BINDING SITE, designated SEQ ID:41439, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46493] Another function of VGAM1314 is therefore inhibition of LOC152200 (Accession XM_098174). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152200. LOC154788 (Accession XM_098607) is another VGAM1314 host target gene. LOC154788 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154788, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154788 BINDING SITE, designated SEQ ID:41726, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46494] Another function of VGAM1314 is therefore inhibition of LOC154788 (Accession XM_098607). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154788. LOC219505 (Accession XM_166086) is another VGAM1314 host target gene. LOC219505 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219505, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219505 BINDING SITE, designated SEQ ID:43853, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46495] Another function of VGAM1314 is therefore inhibition of LOC219505 (Accession XM_166086). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219505. LOC219988 (Accession XM_166223) is another VGAM1314 host target gene. LOC219988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219988 BINDING SITE, designated SEQ ID:44043, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46496] Another function of VGAM1314 is therefore inhibition of LOC219988 (Accession XM_166223). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC219988. LOC222936 (Accession XM_170043) is another VGAM1314 host target gene. LOC222936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222936 BINDING SITE, designated SEQ ID:45309, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46497] Another function of VGAM1314 is therefore inhibition of LOC222936 (Accession XM_170043). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222936. LOC56965 (Accession NM_020213) is another VGAM1314 host target gene. LOC56965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56965 BINDING SITE, designated SEQ ID:21452, to the nucleotide sequence of VGAM1314 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4025.

[46498] Another function of VGAM1314 is therefore inhibition of LOC56965 (Accession NM_020213). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56965. LOC85414 (Accession NM_033102) is another VGAM1314 host target gene. LOC85414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC85414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85414 BINDING SITE, designated SEQ ID:26951, to the nucleotide sequence of VGAM1314 RNA, herein designated VGAM RNA, also designated SEQ ID:4025.

[46499] Another function of VGAM1314 is therefore inhibition of LOC85414 (Accession NM_033102). Accordingly, utilities of VGAM1314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85414. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1315 (VGAM1315) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46500] VGAM1315 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1315 was detected is described hereinabove with reference to Figs. 1–8.

[46501] VGAM1315 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46502] VGAM1315 gene encodes a VGAM1315 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1315 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1315 precursor RNA is designated SEQ ID:1301, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1301 is located at position 7067 relative to the genome of Foot-and-mouth Disease Virus C.

[46503] VGAM1315 precursor RNA folds onto itself, forming

VGAM1315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46504] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1315 folded precursor RNA into VGAM1315 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 86%) nucleotide sequence of VGAM1315 RNA is designated SEQ ID:4026, and is provided hereinbelow with reference to the sequence listing part.

[46505] VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1315 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[46506] VGAM1315 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1315 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1315 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46507] The complementary binding of VGAM1315 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1315 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1315 host target RNA into VGAM1315 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46508] It is appreciated that VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1315 host target genes. The mRNA of each one of this plurality of VGAM1315 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1315 RNA, herein designated VGAM RNA, and which when bound by VGAM1315 RNA causes inhibition of translation of respective one or more VGAM1315 host target proteins.

[46509] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1315 gene, herein designated VGAM GENE, on one or more VGAM1315 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46510] It is yet further appreciated that a function of VGAM1315 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGAM1315 correlate with, and may be deduced from, the identity of the host target genes which VGAM1315 binds

and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46511] Nucleotide sequences of the VGAM1315 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1315 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1315 are further described hereinbelow with reference to Table 1.

[46512] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1315 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1315 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46513] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1315 gene, herein designated VGAM is inhibition of expression of VGAM1315 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1315 correlate with, and may be deduced from, the identity of the target genes which VGAM1315 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[46514] Ca²⁺–dependent Activator Protein For Secretion (CADPS, Accession XM_036915) is a VGAM1315 host target gene. CADPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CADPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CADPS BINDING SITE, designated SEQ ID:32507, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46515] A function of VGAM1315 is therefore inhibition of Ca²⁺–dependent Activator Protein For Secretion (CADPS, Accession XM_036915), a gene which is required for the Ca²⁺–regulated exocytosis of secretory vesicles. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CADPS. The function of CADPS has been established by previous studies. Calcium–activated secretion in neuroendocrine cells is dependent on ATP and cytosolic proteins such as NSF (OMIM Ref. No. 601633), SNAPs (see OMIM Ref. No. 603215) GTP–binding proteins, and com–

ponents of a vesicle coat complex. Walent et al. (1992) isolated a rat cytosolic factor, which they termed p145, that reconstitutes Ca^{2+} -activated secretion via dense core vesicle exocytosis in permeable neuroendocrine cells. The protein is a dimer of 145-kD subunits. By screening rat brain cDNA libraries with anti-p145, Ann et al. (1997) obtained a cDNA encoding a protein of 1,289 amino acids, which they designated CAPS. Sequence analysis revealed an overall hydrophilic protein with 2 potential coiled-coil regions. Northern blot analysis on mRNA from human tissue revealed expression of a 5.6-kb transcript in brain, pancreas, hypothalamus, pituitary, and adrenal, but not in heart, placenta, lung, liver, skeletal muscle, or kidney. The sequence of rat CAPS is 75% similar and 54% identical to that of *C. elegans* UNC31; loss-of-function UNC31 mutants exhibit multiple nervous system defects. Equilibrium dialysis studies showed that CAPS is a calcium-binding protein. By subcellular fractionation of isolated rat presynaptic nerve terminals, or synaptosomes, Berwin et al. (1998) determined that CAPS is primarily associated with plasma membranes and large dense core vesicles but not with small clear synaptic vesicles.

[46516] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [46517] Walent, J. H.; Porter, B. W.; Martin, T. F. J. : A novel 145 kd brain cytosolic protein reconstitutes $\text{Ca}(2+)$ -regulated secretion in permeable neuroendocrine cells. *Cell* 70: 765-775, 1992. ; and
- [46518] Ann, K.; Kowalchuk, J. A.; Loyet, K. M.; Martin, T. F. J. : Novel $\text{Ca}(2+)$ -binding protein (CAPS) related to UNC-31 required for $\text{Ca}(2+)$ -activated exocytosis. *J. Biol. Chem.* 272: 19637-1964.
- [46519] Further studies establishing the function and utilities of CADPS are found in John Hopkins OMIM database record ID 604667, and in cited publications numbered 7478-7481 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin D2 (CCND2, Accession NM_001759) is another VGAM1315 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7515, to the nucleotide sequence of

VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46520] Another function of VGAM1315 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the G1/s (start) transition. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128.EphB4 (EPHB4, Accession NM_004444) is another VGAM1315 host target gene. EPHB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB4 BINDING SITE, designated SEQ ID:10739, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46521] Another function of VGAM1315 is therefore inhibition of EphB4 (EPHB4, Accession NM_004444), a gene which re-

ceptor for members of the ephrin-b family. binds to ephrin-b2. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB4. The function of EPHB4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM808. Lysosomal-associated Membrane Protein 2 (LAMP2, Accession NM_013995) is another VGAM1315 host target gene. LAMP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMP2 BINDING SITE, designated SEQ ID:15185, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46522] Another function of VGAM1315 is therefore inhibition of Lysosomal-associated Membrane Protein 2 (LAMP2, Accession NM_013995). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMP2. LIM Do-

main Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM_005578) is another VGAM1315 host target gene. LPP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPP BINDING SITE, designated SEQ ID:12107, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46523] Another function of VGAM1315 is therefore inhibition of LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM_005578). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPP. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM1315 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of LRP4 BINDING SITE, designated SEQ ID:32200, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46524] Another function of VGAM1315 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Antigen Identified By Monoclonal Antibody MRC OX-2 (MOX2, Accession XM_039962) is another VGAM1315 host target gene. MOX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MOX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOX2 BINDING SITE, designated SEQ ID:33236, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46525] Another function of VGAM1315 is therefore inhibition of Antigen Identified By Monoclonal Antibody MRC OX-2 (MOX2, Accession XM_039962). Accordingly, utilities of

VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOX2. Nebulin-related Anchoring Protein (NRAP, Accession NM_006175) is another VGAM1315 host target gene. NRAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRAP BINDING SITE, designated SEQ ID:12833, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46526] Another function of VGAM1315 is therefore inhibition of Nebulin-related Anchoring Protein (NRAP, Accession NM_006175), a gene which performs an anchoring function to link the terminal actin filaments of myofibrils to protein complexes located beneath the sarcolemma. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRAP. The function of NRAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM649. Pinin, Desmosome

Associated Protein (PNN, Accession XM_048719) is another VGAM1315 host target gene. PNN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PNN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNN BINDING SITE, designated SEQ ID:35232, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46527] Another function of VGAM1315 is therefore inhibition of Pinin, Desmosome Associated Protein (PNN, Accession XM_048719), a gene which reinforces the intermediate filament-desmosome complex. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNN. The function of PNN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM_029842) is another VGAM1315 host target gene. PPT1 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by PPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT1 BINDING SITE, designated SEQ ID:30955, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46528] Another function of VGAM1315 is therefore inhibition of Palmitoyl-protein Thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile) (PPT1, Accession XM_029842). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT1. Sorting Nexin 5 (SNX5, Accession NM_014426) is another VGAM1315 host target gene. SNX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX5 BINDING SITE, designated SEQ ID:15784, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46529] Another function of VGAM1315 is therefore inhibition of

Sorting Nexin 5 (SNX5, Accession NM_014426). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX5. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662) is another VGAM1315 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19195, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46530] Another function of VGAM1315 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 and its association with various diseases and clinical

cal conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Vitronectin (serum spreading factor, somatomedin B, complement S-protein) (VTN, Accession NM_000638) is another VGAM1315 host target gene. VTN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VTN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VTN BINDING SITE, designated SEQ ID:6272, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46531] Another function of VGAM1315 is therefore inhibition of Vitronectin (serum spreading factor, somatomedin B, complement S-protein) (VTN, Accession NM_000638), a gene which is a cell adhesion and spreading factor found in serum and tissues. Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VTN. The function of VTN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM850.Angiomotin (AMOT, Accession NM_133265) is another VGAM1315 host target gene. AMOT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AMOT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOT BINDING SITE, designated SEQ ID:28413, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46532] Another function of VGAM1315 is therefore inhibition of Angiomotin (AMOT, Accession NM_133265). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOT. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 39 (DDX39, Accession NM_138998) is another VGAM1315 host target gene. DDX39 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX39 BINDING SITE, designated SEQ ID:29096, to the nucleotide se-

quence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46533] Another function of VGAM1315 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 39 (DDX39, Accession NM_138998). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX39. DKFZP434K2235 (Accession XM_096869) is another VGAM1315 host target gene. DKFZP434K2235 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434K2235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K2235 BINDING SITE, designated SEQ ID:40594, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46534] Another function of VGAM1315 is therefore inhibition of DKFZP434K2235 (Accession XM_096869). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434K2235. DKFZP564O0423 (Accession

XM_166254) is another VGAM1315 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44063, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46535] Another function of VGAM1315 is therefore inhibition of DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM_014787) is another VGAM1315 host target gene. DNAJC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC6 BINDING SITE, designated SEQ ID:16659, to the nucleotide

sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46536] Another function of VGAM1315 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 6 (DNAJC6, Accession NM_014787). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC6. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 4 (DYRK4, Accession XM_034551) is another VGAM1315 host target gene. DYRK4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DYRK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK4 BINDING SITE, designated SEQ ID:32122, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46537] Another function of VGAM1315 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 4 (DYRK4, Accession XM_034551). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DYRK4. EFA6R (Accession NM_015310) is another VGAM1315 host target gene. EFA6R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFA6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFA6R BINDING SITE, designated SEQ ID:17624, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46538] Another function of VGAM1315 is therefore inhibition of EFA6R (Accession NM_015310). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFA6R. FBP17 (Accession XM_052666) is another VGAM1315 host target gene. FBP17 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36046, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ

ID:4026.

[46539] Another function of VGAM1315 is therefore inhibition of FBP17 (Accession XM_052666). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ10420 (Accession NM_018090) is another VGAM1315 host target gene. FLJ10420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10420 BINDING SITE, designated SEQ ID:19855, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46540] Another function of VGAM1315 is therefore inhibition of FLJ10420 (Accession NM_018090). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10420. FLJ13409 (Accession NM_024617) is another VGAM1315 host target gene. FLJ13409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13409, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13409 BINDING SITE, designated SEQ ID:23878, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46541] Another function of VGAM1315 is therefore inhibition of FLJ13409 (Accession NM_024617). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13409. FLJ13782 (Accession NM_024915) is another VGAM1315 host target gene. FLJ13782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13782 BINDING SITE, designated SEQ ID:24437, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46542] Another function of VGAM1315 is therefore inhibition of FLJ13782 (Accession NM_024915). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13782. FLJ20343 (Accession NM_017775) is another VGAM1315 host target gene. FLJ20343 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20343 BINDING SITE, designated SEQ ID:19399, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46543] Another function of VGAM1315 is therefore inhibition of FLJ20343 (Accession NM_017775). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20343. FLJ21125 (Accession NM_024627) is another VGAM1315 host target gene. FLJ21125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21125 BINDING SITE, designated SEQ ID:23891, to the nucleotide

sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46544] Another function of VGAM1315 is therefore inhibition of FLJ21125 (Accession NM_024627). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21125. FLJ22009 (Accession XM_015700) is another VGAM1315 host target gene. FLJ22009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22009 BINDING SITE, designated SEQ ID:30243, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46545] Another function of VGAM1315 is therefore inhibition of FLJ22009 (Accession XM_015700). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22009. KIAA0987 (Accession NM_012307) is another VGAM1315 host target gene. KIAA0987 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0987 BINDING SITE, designated SEQ ID:14676, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46546] Another function of VGAM1315 is therefore inhibition of KIAA0987 (Accession NM_012307). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0987. MGC19556 (Accession NM_033551) is another VGAM1315 host target gene. MGC19556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC19556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC19556 BINDING SITE, designated SEQ ID:27312, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46547] Another function of VGAM1315 is therefore inhibition of MGC19556 (Accession NM_033551). Accordingly, utilities

of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC19556. VIT1 (Accession NM_018693) is another VGAM1315 host target gene. VIT1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by VIT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIT1 BINDING SITE, designated SEQ ID:20764, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46548] Another function of VGAM1315 is therefore inhibition of VIT1 (Accession NM_018693). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIT1. YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM_014263) is another VGAM1315 host target gene. YME1L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by YME1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of YME1L1 BINDING SITE, designated SEQ ID:15535, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46549] Another function of VGAM1315 is therefore inhibition of YME1-like 1 (*S. cerevisiae*) (YME1L1, Accession NM_014263). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YME1L1. LOC145483 (Accession XM_085156) is another VGAM1315 host target gene. LOC145483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145483 BINDING SITE, designated SEQ ID:37880, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46550] Another function of VGAM1315 is therefore inhibition of LOC145483 (Accession XM_085156). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145483. LOC147649 (Accession XM_085830) is another VGAM1315 host target gene. LOC147649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147649 BINDING SITE, designated SEQ ID:38356, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46551] Another function of VGAM1315 is therefore inhibition of LOC147649 (Accession XM_085830). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147649. LOC151443 (Accession XM_087200) is another VGAM1315 host target gene. LOC151443 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151443 BINDING SITE, designated SEQ ID:39115, to the nucleotide sequence of VGAM1315 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4026.

[46552] Another function of VGAM1315 is therefore inhibition of LOC151443 (Accession XM_087200). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151443. LOC167153 (Accession XM_094312) is another VGAM1315 host target gene. LOC167153 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC167153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC167153 BINDING SITE, designated SEQ ID:40229, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46553] Another function of VGAM1315 is therefore inhibition of LOC167153 (Accession XM_094312). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC167153. LOC220930 (Accession XM_167624) is another VGAM1315 host target gene. LOC220930 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220930, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220930 BINDING SITE, designated SEQ ID:44735, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46554] Another function of VGAM1315 is therefore inhibition of LOC220930 (Accession XM_167624). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220930. LOC220965 (Accession XM_166142) is another VGAM1315 host target gene. LOC220965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220965 BINDING SITE, designated SEQ ID:43946, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46555] Another function of VGAM1315 is therefore inhibition of LOC220965 (Accession XM_166142). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC220965. LOC91286 (Accession XM_037444) is another VGAM1315 host target gene. LOC91286 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91286 BINDING SITE, designated SEQ ID:32621, to the nucleotide sequence of VGAM1315 RNA, herein designated VGAM RNA, also designated SEQ ID:4026.

[46556] Another function of VGAM1315 is therefore inhibition of LOC91286 (Accession XM_037444). Accordingly, utilities of VGAM1315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1316 (VGAM1316) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46557] VGAM1316 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1316 was detected is described hereinabove with reference to Figs. 1–8.

[46558] VGAM1316 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus C. VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46559] VGAM1316 gene encodes a VGAM1316 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1316 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1316 precursor RNA is designated SEQ ID:1302, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1302 is located at position 3523 relative to the genome of Foot-and-mouth Disease Virus C.

[46560] VGAM1316 precursor RNA folds onto itself, forming VGAM1316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46561] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1316 folded precursor RNA into VGAM1316 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1316 RNA is designated SEQ ID:4027, and is provided hereinbelow with reference to the sequence listing part.

[46562] VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1316 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46563] VGAM1316 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1316 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1316 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46564] The complementary binding of VGAM1316 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1316 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1316 host target RNA into VGAM1316 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46565] It is appreciated that VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1316 host target genes. The mRNA of each one of this plurality of VGAM1316 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1316 RNA, herein designated VGAM RNA, and which when bound by VGAM1316 RNA causes inhibition of translation of respective one or more VGAM1316 host target proteins.

[46566] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1316 gene, herein designated VGAM GENE, on one or more VGAM1316 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46567] It is yet further appreciated that a function of VGAM1316 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGAM1316 correlate with, and may be deduced from, the identity of the host target genes which VGAM1316 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46568] Nucleotide sequences of the VGAM1316 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1316 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1316 are further described hereinbelow with reference to Table 1.

[46569] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1316 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1316 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46570] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1316 gene, herein designated VGAM is inhibition of expression of VGAM1316 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1316 correlate with, and may be deduced from, the identity of the target genes which VGAM1316 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46571] Claudin 14 (CLDN14, Accession NM_144492) is a VGAM1316 host target gene. CLDN14 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by CLDN14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN14 BINDING SITE, designated SEQ ID:29309, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46572] A function of VGAM1316 is therefore inhibition of Claudin 14 (CLDN14, Accession NM_144492), a gene which provides structural support for the auditory neuroepithelium. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN14. The function of CLDN14 has been established by previous studies. By sequencing the long arm of chromosome 21, Hattori et al. (2000) identified the CLDN14 gene. Using RACE, Wilcox et al. (2001) amplified a cDNA encoding CLDN14 from human liver cDNA. Comparison of the genomic chromosome 21 sequence with the cDNA sequence indicated that the CLDN14 gene contains 3 exons, and the authors identified 2 splice isoforms, one with and the other without exon 2. Northern blot analysis detected CLDN14 expression in liver and kidney. In situ hybridization and immunofluores-

cence studies revealed mouse Cldn14 expression in the sensory epithelium of the organ of Corti. By sequence analysis of chromosome 21q, Hattori et al. (2000) mapped the CLDN14 gene to 21q22.3. Wilcox et al. (2001) showed that the profound, congenital, recessive deafness segregating in 2 Pakistani families, PKSN6 and PKSR9a, defines a novel locus, DFNB29, on 21q22.1. These families supported maximum 2-point lod scores of 6.7 at theta of zero for the marker D21S1252 and 6.1 at theta of zero for marker D21S2079, respectively. Critical recombinants and homozygosity for polymorphic markers defined a DFNB29 linkage interval of 228,600 bp on 21q22.1. Since the CLDN14 gene maps within the critical interval and was considered a good candidate, Wilcox et al. (2001) examined the sequence of its single protein-coding exon. In affected individuals of family PKSN6, they identified a homozygous 1-bp deletion (398delT; 605608.0001), while in family PKSR9a they identified a val85-to-aspartic acid missense mutation (605608.0002). Val85 is conserved among 12 of the 20 claudins, while isoleucine is present among 5 claudins, and the remaining 3 claudins have either a cysteine or a proline at this position of the consensus molecule. Aspartic acid at position 85 was predicted to af-

fect hydrophobicity and disrupt the predicted secondary structures in transmembrane domain 2.

[46573] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46574] Hattori, M.; Fujiyama, A.; Taylor, T. D.; Watanabe, H.; Yada, T.; Park, H.-S.; Toyoda, A.; Ishii, K.; Totoki, Y.; Choi, D.-K.; Groner, Y.; Soeda, E.; and 52 others : The DNA sequence of human chromosome 21. Nature 405: 311–319, 2000. Note: Erratum: Nature: 407: 110 only, 2000. ; and

[46575] Wilcox, E. R.; Burton, Q. L.; Naz, S.; Riazuddin, S.; Smith, T. N.; Ploplis, B.; Belyatseva, I.; Ben-Yosef, T.; Liburd, N. A.; Morell, R. J.; Kachar, B.; Wu, D. K.; Griffith, A. J.; Ri.

[46576] Further studies establishing the function and utilities of CLDN14 are found in John Hopkins OMIM database record ID 605608, and in cited publications numbered 6766–6767 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ceroid–lipofuscinosis, Neuronal 6, Late Infantile, Variant (CLN6, Accession NM_017882) is another VGAM1316 host target gene. CLN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLN6, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN6 BINDING SITE, designated SEQ ID:19551, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46577] Another function of VGAM1316 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 6, Late Infantile, Variant (CLN6, Accession NM_017882). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN6. C-terminal Binding Protein 1 (CTBP1, Accession XM_042659) is another VGAM1316 host target gene. CTBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTBP1 BINDING SITE, designated SEQ ID:33729, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46578] Another function of VGAM1316 is therefore inhibition of

C-terminal Binding Protein 1 (CTBP1, Accession XM_042659), a gene which binds to cellular and viral transcriptional repressors regulated by NAD⁺ and NADH. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTBP1. The function of CTBP1 has been established by previous studies. Polycomb (Pc) is part of a Pc group (PcG) protein complex that is involved in repression of gene activity during *Drosophila* and vertebrate development. Using a yeast 2-hybrid assay, Sewalt et al. (1999) found that *Xenopus* Ctbp1 interacts with *Xenopus* Pc and that human CTBP2 interacts with PC2 (OMIM Ref. No. 603079), a human Pc homolog. Immunofluorescence studies indicated that CTBP1 and CTBP2 partially colocalize with PC2 in large PcG domains in interphase nuclei. As with PC2, chimeric LexA-CTBP2 and LexA-CTBP1 proteins repressed gene activity when targeted to a reporter gene. Sewalt et al. (1999) suggested that PC2-mediated repression of gene expression involves an association with corepressors such as the CTBPs. They speculated that the interference of the adenoviral E1A protein with the transcription machinery of the infected cell may involve interference with PcG-mediated repres-

sion through disruption of the CTBP–PcG interaction.

Northern blot analysis revealed that the CTBP1 gene was expressed as a 2.4–kb mRNA in all human tissues tested. Zhang et al. (2002) demonstrated that CTBP binding to cellular and viral transcriptional repressors is regulated by NAD⁺ and NADH, with NADH being 2 to 3 orders of magnitude more effective. Levels of free nuclear nicotinamide adenine dinucleotides, determined using 2–photon microscopy, corresponded to the levels required for half-maximal CTBP binding and were considerably lower than those previously reported. Agents capable of increasing NADH levels stimulated CTBP binding to its partners in vivo and potentiated CTBP–mediated repression. Zhang et al. (2002) proposed that this ability to detect changes in nuclear NAD⁺/NADH ratio allows CTBP to serve as a redox sensor for transcription.

[46579] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46580] Sewalt, R. G. A. B.; Gunster, M. J.; van der Vlag, J.; Satijn, D. P. E.; Otte, A. P. : C-terminal binding protein is a transcriptional repressor that interacts with a specific class of vertebrate polycomb proteins. *Molec. Cell. Biol.* 19:

777-787, 1999. ; and

[46581] Zhang, Q.; Piston, D. W.; Goodman, R. H. : Regulation of corepressor function by nuclear NADH. Science 295: 1895-1897, 2002.

[46582] Further studies establishing the function and utilities of CTBP1 are found in John Hopkins OMIM database record ID 602618, and in cited publications numbered 8463-8468 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome X Open Reading Frame 6 (CXorf6, Accession NM_005491) is another VGAM1316 host target gene. CXorf6 BINDING SITE1 and CXorf6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CXorf6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf6 BINDING SITE1 and CXorf6 BINDING SITE2, designated SEQ ID:11993 and SEQ ID:11992 respectively, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46583] Another function of VGAM1316 is therefore inhibition of Chromosome X Open Reading Frame 6 (CXorf6, Accession

NM_005491). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf6. Dihydrofolate Reductase (DHFR, Accession NM_000791) is another VGAM1316 host target gene. DHFR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DHFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHFR BINDING SITE, designated SEQ ID:6449, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46584] Another function of VGAM1316 is therefore inhibition of Dihydrofolate Reductase (DHFR, Accession NM_000791), a gene which converts dihydrofolate into tetrahydrofolate. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHFR. The function of DHFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM826.Folylpolyglutamate Synthase (FPGS, Accession

NM_004957) is another VGAM1316 host target gene. FPGS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FPGS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FPGS BINDING SITE, designated SEQ ID:11402, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46585] Another function of VGAM1316 is therefore inhibition of Folylpolyglutamate Synthase (FPGS, Accession NM_004957), a gene which is involved in conversion of folates to polyglutamate derivatives. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FPGS. The function of FPGS has been established by previous studies. By functional complementation of an *Escherichia coli* folC mutant, Garrow et al. (1992) cloned a human cDNA for folylpoly(γ -glutamate) synthetase (FPGS; tetrahydrofolate:L-glutamate γ -ligase (ADP forming); EC 6.3.2.17). The cDNA encodes a 545-residue protein of Mr 60,128. Expression of the cDNA in *E. coli* resulted in elevated expression of an enzyme with charac-

teristics of mammalian FPGS. Furthermore, expression of the cDNA in AUXB1, a mammalian cell lacking FPGS activity, overcame the cell's requirement for thymidine and purines but did not overcome the cell's glycine auxotrophy, consistent with expression of the protein in the cytosol but not in the mitochondria. Freemantle et al. (1995) proposed that the mitochondrial and cytosolic forms of FPGS are, in fact, derived from the same gene, arising from the use of the 2 different translation initiation codons, and that the translation products differ by the presence of a 42-residue amino-terminal mitochondrial leader peptide. Taylor et al. (1995) likewise concluded that a single locus encodes FPGS-related sequences in the human genome. The complete 2256 nucleotides of cDNA for the 5-prime untranslated region, mitochondrial leader sequence, coding region, and 3-prime untranslated region were found to be distributed on 15 exons stretching over 11.2 kb of genomic DNA.

[46586] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46587] Freemantle, S. J.; Taylor, S. M.; Krystal, G.; Moran, R. G. : Upstream organization of and multiple transcripts from

the human folylpoly- γ -glutamate synthetase gene.

J. Biol. Chem. 270: 9579-9584, 1995. ; and

[46588] Garrow, T. A.; Admon, A.; Shane, B. : Expression cloning of a human cDNA encoding folylpoly(γ -glutamate) synthetase and determination of its primary structure. Proc. Nat. Acad. Sci.

[46589] Further studies establishing the function and utilities of FPGS are found in John Hopkins OMIM database record ID 136510, and in cited publications numbered 11763-11771 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glypican 1 (GPC1, Accession NM_002081) is another VGAM1316 host target gene. GPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC1 BINDING SITE, designated SEQ ID:7873, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46590] Another function of VGAM1316 is therefore inhibition of Glypican 1 (GPC1, Accession NM_002081), a gene which

may play a role in growth control and differentiation. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC1. The function of GPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 4 (HCN4, Accession NM_005477) is another VGAM1316 host target gene. HCN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HCN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCN4 BINDING SITE, designated SEQ ID:11978, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46591] Another function of VGAM1316 is therefore inhibition of Hyperpolarization Activated Cyclic Nucleotide-gated Potassium Channel 4 (HCN4, Accession NM_005477), a gene which is hyperpolarization activated cyclic nucleotide-gated cation channel 4 and may act as a pace-

maker channel in the heart . Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCN4. The function of HCN4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Lymphotoxin Beta Receptor (TNFR superfamily, member 3) (LTBR, Accession NM_002342) is another VGAM1316 host target gene. LTBR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LTBR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTBR BINDING SITE, designated SEQ ID:8141, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46592] Another function of VGAM1316 is therefore inhibition of Lymphotoxin Beta Receptor (TNFR superfamily, member 3) (LTBR, Accession NM_002342), a gene which is a receptor for the heterotrimeric lymphotoxin containing lta and ltb, and for tnfs14/light. promotes apoptosis via traf3 and traf5. may play a role in the development of lymphoid or-

gans. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTBR. The function of LTBR has been established by previous studies. Crowe et al. (1994) demonstrated that the tumor necrosis factor receptor related protein is the human receptor for the heterotrimer of lymphotoxin-alpha (OMIM Ref. No. 153440) and lymphotoxin-beta (OMIM Ref. No. 600978). This LT-alpha/LT-beta heterotrimer is assumed to take part in immunologic reactions by cell-cell contact, but does not bind to either TNFR1 (OMIM Ref. No. 191190) or TNFR2 (OMIM Ref. No. 191191). Nakamura et al. (1995) isolated the LT-beta receptor cDNA from a cDNA library of murine embryonic heart mRNA, using the signal sequence trap (SST) method, a newly developed strategy for cloning secreted proteins and type I membrane proteins (Tashiro et al., 1993). This method, which does not require specific functional assays, takes advantage of the fact that their precursors carry amino-terminal signal sequences. The deduced amino acid sequence of the mouse LT-beta receptor is 66% identical to that of the human protein. Northern analysis of various organs in adult mice have showed that expression levels of LTBR mRNA were strong

in lung, liver, and kidney, moderate in heart and testes, but weak in brain, thymus, spleen, and lymph nodes.

Nakamura et al. (1995) speculated that, since the mouse receptor was already expressed in 7 day-postcoitus embryos, the LT-alpha/LT-beta receptor system may have some function in early embryogenesis. By linkage analysis with recombinant inbred mouse strains, Nakamura et al. (1995) demonstrated that the locus, designated Tnfr, is very close to the Tnfr1 gene on mouse chromosome 6.

Presumably, the human homolog is located on 12p13

[46593] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46594] Crowe, P. D.; VanArsdale, T. L.; Walter, B. N.; Ware, C. F.; Hession, C.; Ehrenfels, B.; Browning, J. L.; Din, W. S.; Goodwin, R. G; Smith, C. A. : A lymphotoxin-beta-specific receptor. Science 264: 707-710, 1994. ; and

[46595] Nakamura, T.; Tashiro, K.; Nazarea, M.; Nakano, T.; Sasayama, S.; Honjo, T. : The murine lymphotoxin-beta receptor cDNA: isolation by the signal sequence trap and chromosomal mapping. Gen.

[46596] Further studies establishing the function and utilities of LTBR are found in John Hopkins OMIM database record ID

600979, and in cited publications numbered 7804–7806 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. NADH Dehydrogenase (ubiquinone) Flavoprotein 3, 10kDa (NDUFV3, Accession NM_021075) is another VGAM1316 host target gene. NDUFV3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NDUFV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDUFV3 BINDING SITE, designated SEQ ID:22045, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46597] Another function of VGAM1316 is therefore inhibition of NADH Dehydrogenase (ubiquinone) Flavoprotein 3, 10kDa (NDUFV3, Accession NM_021075), a gene which transports electrons from NADH to ubiquinone. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDUFV3. The function of NDUFV3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to

VGAM626.6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (PFKFB4, Accession NM_004567) is another VGAM1316 host target gene. PFKFB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFKFB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFKFB4 BINDING SITE, designated SEQ ID:10909, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46598] Another function of VGAM1316 is therefore inhibition of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 4 (PFKFB4, Accession NM_004567), a gene which catalyzes synthesis and degradation of fructose 2,6-bisphosphate. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFKFB4. The function of PFKFB4 has been established by previous studies. The bifunctional 6-phosphofructo-2-kinase (EC 2.7.1.105)/fructose-2,6-bisphosphatase (EC 3.1.3.46) (PFKFB) regulates the steady-state concentration of fruc-

tose-2,6-bisphosphate, a potent activator of a key regulatory enzyme of glycolysis, phosphofructokinase.

Isozymes of PFKFB differ in the regions surrounding the catalytic core, which are important for the differential response to allosteric effectors and hormonal signals in different tissues. By screening a placental cDNA library with human and frog liver PFKFB (PFKFB1; 311790) as probes, Sakai et al. (1996) obtained a partial cDNA encoding PFKFB4, which they termed 2K-1. Manzano et al. (1999) isolated a cDNA encoding PFKFB4 by screening a human testis cDNA library with a rat liver Pfkfb probe, followed by RT-PCR. The predicted 469-amino acid PFKFB4 protein, which is 97% homologous to the rat sequence and approximately 70% identical to the human PFKFB isoforms, contains multiple phosphorylation sites. Northern blot analysis of rat brain, heart, liver, muscle, placenta, adipose tissue, ovary, fallopian tubes, and testis with the human PFKFB4 sequence as probe detected testis-specific expression of 2.4- and 3.3-kb transcripts. Western blot analysis showed expression of a 55-kD protein, close to the predicted value.

[46599] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [46600] Sakai, A.; Kato, M.; Fukasawa, M.; Ishiguro, M.; Furuya, E.; Sakakibara, R. : Cloning of cDNA encoding for a novel isozyme of fructose 6-phosphate,2-kinase/fructose 2,6-bisphosphatase from human placenta. J. Biochem. 119: 506-511, 1996. ; and
- [46601] Manzano, A.; Perez, J. X.; Nadal, M.; Estivill, X.; Lange, A.; Bartrons, R. : Cloning, expression and chromosomal localization of a human testis 6-phosphofructo-2-kinase/fructose-2,6-bis.
- [46602] Further studies establishing the function and utilities of PFKFB4 are found in John Hopkins OMIM database record ID 605320, and in cited publications numbered 4491 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TAL1 (SCL) Interrupting Locus (SIL, Accession NM_003035) is another VGAM1316 host target gene. SIL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIL BINDING SITE, designated SEQ ID:8985, to the nucleotide sequence of

VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46603] Another function of VGAM1316 is therefore inhibition of TAL1 (SCL) Interrupting Locus (SIL, Accession NM_003035), a gene which may be required for axial development and left-right specification. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIL. The function of SIL has been established by previous studies. Aplan et al. (1997) demonstrated that transgenic mice in which inappropriately expressed scl protein, driven by sil regulatory elements, developed aggressive T-cell malignancies in collaboration with a mis-expressed LMO1 (OMIM Ref. No. 186921) protein, thus recapitulating the situation seen in a subset of human T-cell ALL. Aplan et al. (1997) also demonstrated that inappropriately expressed scl can interfere with the development of other tissues derived from mesoderm. Finally, Aplan et al. (1997) demonstrated that an scl construct lacking the scl transactivation domain collaborates with misexpressed LMO1, demonstrating that the scl transactivation domain is dispensable for oncogenesis, and supporting the hypothesis that the scl gene product exerts its

oncogenic action through a dominant-negative mechanism. Animal model experiments lend further support to the function of SIL. Izraeli et al. (1999) disrupted the Sil gene in mouse by homologous recombination. Heterozygotes were normal but mutant homozygotes died in utero after embryonic day 10.5. Between embryonic days 7.5 and 8.5, striking developmental anomalies appeared in Sil $-/-$ embryos. In addition to reduced size and limited developmental progress compared to wildtype embryos, Sil mutants displayed prominent midline neural tube defects. These included delay or failure of neural tube closure and holoprosencephaly (OMIM Ref. No. 236100). In addition, left-right development was abnormal. In heterozygous and wildtype embryos, the embryonic heart tube always loops to the right, whereas in Sil mutants the direction of heart looping is randomized. Nodal (OMIM Ref. No. 601265), lefty-2 (OMIM Ref. No. 603037) and Pitx2 (OMIM Ref. No. 601542) are normally expressed only in the left lateral-plate mesoderm before heart looping, with continued expression of Pitx2 on the left side of the looping heart tube. In contrast, Sil mutants showed bilaterally symmetric expression of nodal and Pitx2 at all stages examined. For lefty-2, most Sil $-/-$ embryos also showed bi-

laterally symmetric expression. However, a small number of mutants expressed lefty-2 only on the right. Expression of both Patched (OMIM Ref. No. 601309) and Gli1 (OMIM Ref. No. 165220) was greatly reduced in Sil -/- embryos. Shh (OMIM Ref. No. 600725) and Hnf3b (OMIM Ref. No. 600288) were expressed in the notochord of Sil mutants. However, the markedly reduced expression of their target genes indicated that Shh signaling in the midline may be blocked in Sil -/- embryos. Comparison with Shh mutant embryos, which have axial defects but normal cardiac looping, indicated that the consequences of abnormal midline development for left-right patterning depend on the time of onset, duration, and severity of disruption of the normal asymmetric patterns of expression of nodal, lefty-2, and Pitx2.

[46604] It is appreciated that the abovementioned animal model for SIL is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[46605] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46606] Aplan, P. D.; Jones, C. A.; Chervinsky, D. S.; Zhao, X.;

Ellsworth, M.; Wu, C.; McGuire, E. A.; Gross, K. W. : An scl gene product lacking the transactivation domain induces bony abnormalities and cooperates with LMO1 to generate T-cell malignancies in transgenic mice. EMBO J. 16: 2408–2419, 1997. ; and

[46607] Izraeli, S.; Lowe, L. A.; Bertness, V. L.; Good, D. J.; Dorward, D. W.; Kirsch, I. R.; Kuehn, M. R. : The SIL gene is required for mouse embryonic axial development and left-right spec.

[46608] Further studies establishing the function and utilities of SIL are found in John Hopkins OMIM database record ID 181590, and in cited publications numbered 12610–12615 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SRY (sex determining region Y)–box 4 (SOX4, Accession NM_003107) is another VGAM1316 host target gene. SOX4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SOX4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX4 BINDING SITE, designated SEQ ID:9072, to the nucleotide sequence of VGAM1316 RNA, herein

designated VGAM RNA, also designated SEQ ID:4027.

[46609] Another function of VGAM1316 is therefore inhibition of SRY (sex determining region Y)-box 4 (SOX4, Accession NM_003107), a gene which binds with high affinity to the t-cell enhancer motif 5'-aacaaag-3' motif. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX4. The function of SOX4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM409. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM1316 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE, designated SEQ ID:11067, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46610] Another function of VGAM1316 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene

which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. TAF7 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 55kDa (TAF7, Accession NM_005642) is another VGAM1316 host target gene. TAF7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TAF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAF7 BINDING SITE, designated SEQ ID:12176, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46611] Another function of VGAM1316 is therefore inhibition of TAF7 RNA Polymerase II, TATA Box Binding Protein (TBP)–associated Factor, 55kDa (TAF7, Accession NM_005642), a gene which may function as a coactivator of transcription with some activators. Accordingly, utilities

of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF7. The function of TAF7 has been established by previous studies. Chiang and Roeder (1995) reported the cloning of a subunit of the TFIID protein complex (OMIM Ref. No. 313650) which is required for transcription by promoters targeted by RNA polymerase II. The TFIID complex binds to the TATA box in class II promoters and then recruits other factors as well as RNA polymerase II. TFIID is composed of the TATA-binding protein (TBP; 600075) and multiple TBP-associated factors (TAFs), one of which has a predicted size of 55 kD from SDS gel electrophoresis. The human TFIID subunit TAF2F (also referred to as TAFII55) was isolated from a cell line that expresses an epitope-tagged TBP allowing for the immunoprecipitation of the TFIID complex and associated factors. Based on partial peptide sequence of 1 TAF, Chiang and Roeder (1995) designed degenerate PCR primers and used them to produce a probe which was, in turn, hybridized to a human placenta cDNA library. The predicted protein is 349 amino acids (40 kD) and contains 40% charged residues, which may account for its larger than expected electrophoretic mobility. The mRNA was expressed in all

tissues examined. The authors showed that TAFII55 interacts with TAFII230, the largest subunit of TFIID, and with multiple transcription activators, including Sp1 (OMIM Ref. No. 189906), YY1 (OMIM Ref. No. 600013), USF (OMIM Ref. No. 191523), CTF (600729; discussed also in 164005), and adenoviral E1A (discussed in 607102). By genomic sequence analysis, Wu et al. (2001) determined that the mouse and human TAF2F genes contain a single exon.

[46612] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46613] Chiang, C.-M.; Roeder, R. G. : Cloning of an intrinsic human TFIID subunit that interacts with multiple transcriptional activators. *Science* 267: 531–536, 1995. ; and

[46614] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse an.

[46615] Further studies establishing the function and utilities of TAF7 are found in John Hopkins OMIM database record ID 600573, and in cited publications numbered 9534–9535 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. Thrombospondin 1 (THBS1, Accession NM_003246) is another VGAM1316 host target gene. THBS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by THBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBS1 BINDING SITE, designated SEQ ID:9255, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46616] Another function of VGAM1316 is therefore inhibition of Thrombospondin 1 (THBS1, Accession NM_003246), a gene which is a member of a family of adhesive molecules, involves in blood clotting and in angiogenesis. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBS1. The function of THBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM20. Tuftelin 1 (TUFT1, Accession NM_020127) is another VGAM1316 host target gene. TUFT1 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by TUFT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUFT1 BINDING SITE, designated SEQ ID:21316, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46617] Another function of VGAM1316 is therefore inhibition of Tuftelin 1 (TUFT1, Accession NM_020127), a gene which appears to play a role in cytokinesis, cell shape, and specialized functions such as secretion and capping. Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUFT1. The function of TUFT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1152. A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 10 (ADAMTS10, Accession NM_030957) is another VGAM1316 host target gene. ADAMTS10 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by

ADAMTS10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS10 BINDING SITE, designated SEQ ID:25231, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46618] Another function of VGAM1316 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 10 (ADAMTS10, Accession NM_030957). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS10. BRAG (Accession NM_014863) is another VGAM1316 host target gene. BRAG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BRAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRAG BINDING SITE, designated SEQ ID:16942, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46619] Another function of VGAM1316 is therefore inhibition of

BRAG (Accession NM_014863). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRAG. DKFZP762D096 (Accession XM_037662) is another VGAM1316 host target gene. DKFZP762D096 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP762D096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP762D096 BINDING SITE, designated SEQ ID:32665, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46620] Another function of VGAM1316 is therefore inhibition of DKFZP762D096 (Accession XM_037662). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP762D096. FASTK (Accession NM_025096) is another VGAM1316 host target gene. FASTK BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FASTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FASTK BINDING SITE, designated SEQ ID:24729, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46621] Another function of VGAM1316 is therefore inhibition of FASTK (Accession NM_025096). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FASTK. FLJ10898 (Accession XM_002486) is another VGAM1316 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29894, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46622] Another function of VGAM1316 is therefore inhibition of FLJ10898 (Accession XM_002486). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10898. FLJ12800 (Accession NM_022903) is another VGAM1316 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800 BINDING SITE, designated SEQ ID:23192, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46623] Another function of VGAM1316 is therefore inhibition of FLJ12800 (Accession NM_022903). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ21709 (Accession XM_085480) is another VGAM1316 host target gene. FLJ21709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21709 BINDING SITE, designated SEQ ID:38168, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM

RNA, also designated SEQ ID:4027.

[46624] Another function of VGAM1316 is therefore inhibition of FLJ21709 (Accession XM_085480). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21709. Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424) is another VGAM1316 host target gene. HSPB7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPB7 BINDING SITE, designated SEQ ID:15782, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46625] Another function of VGAM1316 is therefore inhibition of Heat Shock 27kDa Protein Family, Member 7 (cardiovascular) (HSPB7, Accession NM_014424). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPB7. KIAA0087 (Accession NM_014769) is another VGAM1316 host target gene. KIAA0087 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0087 BINDING SITE, designated SEQ ID:16556, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46626] Another function of VGAM1316 is therefore inhibition of KIAA0087 (Accession NM_014769). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0087. KIAA0318 (Accession XM_044334) is another VGAM1316 host target gene. KIAA0318 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0318 BINDING SITE, designated SEQ ID:34188, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46627] Another function of VGAM1316 is therefore inhibition of

KIAA0318 (Accession XM_044334). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0318. KIAA0545 (Accession XM_032278) is another VGAM1316 host target gene. KIAA0545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0545 BINDING SITE, designated SEQ ID:31636, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46628] Another function of VGAM1316 is therefore inhibition of KIAA0545 (Accession XM_032278). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0545. KIAA1322 (Accession XM_052626) is another VGAM1316 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36028, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46629] Another function of VGAM1316 is therefore inhibition of KIAA1322 (Accession XM_052626). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. KIAA1719 (Accession XM_042936) is another VGAM1316 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33818, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46630] Another function of VGAM1316 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. KIAA1924 (Accession XM_057091) is another

VGAM1316 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36477, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46631] Another function of VGAM1316 is therefore inhibition of KIAA1924 (Accession XM_057091). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1924. Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM_012316) is another VGAM1316 host target gene. KPNA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KPNA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KPNA6 BINDING SITE, designated SEQ ID:14688, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4027.

[46632] Another function of VGAM1316 is therefore inhibition of Karyopherin Alpha 6 (importin alpha 7) (KPNA6, Accession NM_012316). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KPNA6. MGC10812 (Accession NM_031425) is another VGAM1316 host target gene. MGC10812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10812 BINDING SITE, designated SEQ ID:25413, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46633] Another function of VGAM1316 is therefore inhibition of MGC10812 (Accession NM_031425). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10812. MGC15827 (Accession NM_032882) is another VGAM1316 host target gene. MGC15827 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by MGC15827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15827 BINDING SITE, designated SEQ ID:26702, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46634] Another function of VGAM1316 is therefore inhibition of MGC15827 (Accession NM_032882). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15827. MR (Accession NM_031212) is another VGAM1316 host target gene. MR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MR BINDING SITE, designated SEQ ID:25255, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46635] Another function of VGAM1316 is therefore inhibition of MR (Accession NM_031212). Accordingly, utilities of

VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MR.

Tripartite Motif-containing 2 (TRIM2, Accession NM_015271) is another VGAM1316 host target gene.

TRIM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM2 BINDING SITE, designated SEQ ID:17600, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46636] Another function of VGAM1316 is therefore inhibition of Tripartite Motif-containing 2 (TRIM2, Accession NM_015271). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM2. LOC199964 (Accession XM_117165) is another VGAM1316 host target gene. LOC199964 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199964 BINDING SITE, designated SEQ ID:43267, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46637] Another function of VGAM1316 is therefore inhibition of LOC199964 (Accession XM_117165). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199964. LOC199986 (Accession XM_117168) is another VGAM1316 host target gene. LOC199986 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199986 BINDING SITE, designated SEQ ID:43273, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46638] Another function of VGAM1316 is therefore inhibition of LOC199986 (Accession XM_117168). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC199986. LOC220549 (Accession XM_167521) is another VGAM1316 host target gene. LOC220549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220549 BINDING SITE, designated SEQ ID:44651, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46639] Another function of VGAM1316 is therefore inhibition of LOC220549 (Accession XM_167521). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220549. LOC254532 (Accession XM_172961) is another VGAM1316 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46211, to the nucleotide sequence of VGAM1316 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4027.

[46640] Another function of VGAM1316 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC90917 (Accession XM_034861) is another VGAM1316 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32169, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46641] Another function of VGAM1316 is therefore inhibition of LOC90917 (Accession XM_034861). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90917. LOC91409 (Accession XM_038298) is another VGAM1316 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32801, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46642] Another function of VGAM1316 is therefore inhibition of LOC91409 (Accession XM_038298). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. LOC91948 (Accession XM_041723) is another VGAM1316 host target gene. LOC91948 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91948 BINDING SITE, designated SEQ ID:33572, to the nucleotide sequence of VGAM1316 RNA, herein designated VGAM RNA, also designated SEQ ID:4027.

[46643] Another function of VGAM1316 is therefore inhibition of LOC91948 (Accession XM_041723). Accordingly, utilities of VGAM1316 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC91948. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1317 (VGAM1317) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46644] VGAM1317 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1317 was detected is described hereinabove with reference to Figs. 1–8.

[46645] VGAM1317 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus O. VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46646] VGAM1317 gene encodes a VGAM1317 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1317 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1317 precursor RNA is desig-

nated SEQ ID:1303, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1303 is located at position 1129 relative to the genome of Foot-and-mouth Disease Virus O.

- [46647] VGAM1317 precursor RNA folds onto itself, forming VGAM1317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46648] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1317 folded precursor RNA into VGAM1317 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1317 RNA is designated SEQ ID:4028, and is provided hereinbelow with reference to the sequence

listing part.

[46649] VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1317 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46650] VGAM1317 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1317 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1317 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46651] The complementary binding of VGAM1317 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1317 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1317 host target RNA into VGAM1317 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46652] It is appreciated that VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1317 host target genes. The mRNA of each one of this plurality of VGAM1317 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1317 RNA, herein designated VGAM

RNA, and which when bound by VGAM1317 RNA causes inhibition of translation of respective one or more VGAM1317 host target proteins.

[46653] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1317 gene, herein designated VGAM GENE, on one or more VGAM1317 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46654] It is yet further appreciated that a function of VGAM1317 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1317 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus O. Specific functions, and accordingly utilities, of VGAM1317 correlate with, and may be deduced from, the identity of the host target genes which VGAM1317 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46655] Nucleotide sequences of the VGAM1317 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1317 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1317 are further described hereinbelow with reference to Table 1.

[46656] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1317 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1317 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46657] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1317 gene, herein designated VGAM is

inhibition of expression of VGAM1317 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1317 correlate with, and may be deduced from, the identity of the target genes which VGAM1317 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46658] Uncoupling Protein 3 (mitochondrial, proton carrier) (UCP3, Accession NM_003356) is a VGAM1317 host target gene. UCP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UCP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UCP3 BINDING SITE, designated SEQ ID:9384, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46659] A function of VGAM1317 is therefore inhibition of Uncoupling Protein 3 (mitochondrial, proton carrier) (UCP3, Accession NM_003356), a gene which is a mitochondrial transporter protein that creates proton leaks across the inner mitochondrial membrane, thus uncoupling oxidative phosphorylation. Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with UCP3. The function of UCP3 has been established by previous studies. With the capacity to participate in thermogenesis and energy balance, UCP3 is an important obesity candidate gene.

Bouchard et al. (1997) demonstrated linkage between markers at the UCP2/UCP3 region with resting metabolic rate. This region is syntenic to a region of mouse chromosome 7 that has been linked to hyperinsulinemia and obesity (Fleury et al., 1997). Animal model experiments lend further support to the function of UCP3. Clapham et al. (2000) created transgenic mice that overexpress human UCP3 in skeletal muscle. UCP3 expression was driven by the human alpha-skeletal actin (OMIM Ref. No. 102610) promoter, limiting expression to skeletal muscle. Clapham et al. (2000) bred 3 independent lines to homozygosity and selected a line of mice that had a 66-fold increase in UCP3 expression. These mice were hyperphagic but weighed less than their wildtype littermates. Magnetic resonance imaging (MRI) showed a striking reduction in adipose tissue mass. The mice also exhibited lower fasting plasma glucose and insulin levels and an increased glucose clearance rate. Clapham et al. (2000) concluded that their data provided evidence that skeletal muscle

UCP3 has the potential to influence metabolic rates and glucose homeostasis in the whole animal.

[46660] It is appreciated that the abovementioned animal model for UCP3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[46661] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46662] Clapham, J. C.; Arch, J. R. S.; Chapman, H.; Haynes, A.; Lister, C.; Moore, G. B. T.; Piercy, V.; Carter, S. A.; Lehner, I.; Smith, S. A.; Beeley, L. J.; Godden, R. J.; and 15 others : Mice overexpressing human uncoupling protein-3 in skeletal muscle are hyperphagic and lean. *Nature* 406: 415-418, 2000. ; and

[46663] Fleury, C.; Neverova, M.; Collins, S.; Raimbault, S.; Champigny, O.; Levi-Meyrueis, C.; Bouillaud, F.; Seldin, M. F.; Surwit, R. S.; Ricquier, D.; Warden, C. H. : Uncoupling protein-2.

[46664] Further studies establishing the function and utilities of UCP3 are found in John Hopkins OMIM database record ID 602044, and in cited publications numbered 6660-6662, 6484, 6663, 5960-5961, 3700, 6487, 6489, 8525-852

and 2794 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDC10 Cell Division Cycle 10 Homolog (*S. cerevisiae*) (CDC10, Accession XM_165879) is another VGAM1317 host target gene. CDC10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC10 BINDING SITE, designated SEQ ID:43792, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46665] Another function of VGAM1317 is therefore inhibition of CDC10 Cell Division Cycle 10 Homolog (*S. cerevisiae*) (CDC10, Accession XM_165879). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC10. FLJ10716 (Accession NM_018191) is another VGAM1317 host target gene. FLJ10716 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10716, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10716 BINDING SITE, designated SEQ ID:20045, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46666] Another function of VGAM1317 is therefore inhibition of FLJ10716 (Accession NM_018191). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10716. KIAA0976 (Accession NM_014917) is another VGAM1317 host target gene. KIAA0976 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0976 BINDING SITE, designated SEQ ID:17165, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46667] Another function of VGAM1317 is therefore inhibition of KIAA0976 (Accession NM_014917). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0976. KIAA1136 (Accession XM_166110) is another VGAM1317 host target gene. KIAA1136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1136 BINDING SITE, designated SEQ ID:43882, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46668] Another function of VGAM1317 is therefore inhibition of KIAA1136 (Accession XM_166110). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1136. Ubiquitin-conjugating Enzyme E2 Variant 2 (UBE2V2, Accession NM_003350) is another VGAM1317 host target gene. UBE2V2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2V2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V2 BINDING SITE, designated SEQ ID:9375, to the nucleotide sequence of

VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46669] Another function of VGAM1317 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 2 (UBE2V2, Accession NM_003350). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V2.

LOC121274 (Accession XM_058547) is another VGAM1317 host target gene. LOC121274 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121274 BINDING SITE, designated SEQ ID:36655, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46670] Another function of VGAM1317 is therefore inhibition of LOC121274 (Accession XM_058547). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121274. LOC121536 (Accession XM_058567) is another VGAM1317 host target gene. LOC121536 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC121536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121536 BINDING SITE, designated SEQ ID:36662, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46671] Another function of VGAM1317 is therefore inhibition of LOC121536 (Accession XM_058567). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121536. LOC151201 (Accession XM_098021) is another VGAM1317 host target gene. LOC151201 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151201 BINDING SITE, designated SEQ ID:41319, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46672] Another function of VGAM1317 is therefore inhibition of

LOC151201 (Accession XM_098021). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151201. LOC152282 (Accession XM_087435) is another VGAM1317 host target gene. LOC152282 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152282, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152282 BINDING SITE, designated SEQ ID:39254, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46673] Another function of VGAM1317 is therefore inhibition of LOC152282 (Accession XM_087435). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152282. LOC254312 (Accession XM_172839) is another VGAM1317 host target gene. LOC254312 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC254312 BINDING SITE, designated SEQ ID:46114, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46674] Another function of VGAM1317 is therefore inhibition of LOC254312 (Accession XM_172839). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254312. LOC254413 (Accession XM_173141) is another VGAM1317 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46401, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46675] Another function of VGAM1317 is therefore inhibition of LOC254413 (Accession XM_173141). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC90288 (Accession XM_030669) is an-

other VGAM1317 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31107, to the nucleotide sequence of VGAM1317 RNA, herein designated VGAM RNA, also designated SEQ ID:4028.

[46676] Another function of VGAM1317 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities of VGAM1317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1318 (VGAM1318) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46677] VGAM1318 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1318 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[46678] VGAM1318 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus O. VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46679] VGAM1318 gene encodes a VGAM1318 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1318 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1318 precursor RNA is designated SEQ ID:1304, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1304 is located at position 7392 relative to the genome of Foot-and-mouth Disease Virus O.

[46680] VGAM1318 precursor RNA folds onto itself, forming VGAM1318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46681] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1318 folded precursor RNA into VGAM1318 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1318 RNA is designated SEQ ID:4029, and is provided hereinbelow with reference to the sequence listing part.

[46682] VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1318 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46683] VGAM1318 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1318 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1318 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1318 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46684] The complementary binding of VGAM1318 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1318 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1318 host target RNA into VGAM1318 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46685] It is appreciated that VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1318 host target genes. The mRNA of each one of this plurality of VGAM1318 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1318 RNA, herein designated VGAM RNA, and which when bound by VGAM1318 RNA causes inhibition of translation of respective one or more VGAM1318 host target proteins.

[46686] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1318 gene, herein designated VGAM GENE, on one or more VGAM1318 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46687] It is yet further appreciated that a function of VGAM1318 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1318 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus O. Specific functions, and accordingly utilities, of VGAM1318 correlate with, and may be deduced from, the identity of the host target genes which VGAM1318 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46688] Nucleotide sequences of the VGAM1318 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1318 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1318 are further described hereinbelow with reference to Table 1.

[46689] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1318 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1318 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46690] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1318 gene, herein designated VGAM is inhibition of expression of VGAM1318 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1318 correlate with, and may be deduced from, the identity of the target genes which VGAM1318 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46691] Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM_005667) is a VGAM1318 host target gene. ZFP103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZFP103, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP103 BINDING SITE, designated SEQ ID:12220, to the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, also designated SEQ ID:4029.

[46692] A function of VGAM1318 is therefore inhibition of Zinc Finger Protein 103 Homolog (mouse) (ZFP103, Accession NM_005667). Accordingly, utilities of VGAM1318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP103. FLJ11850 (Accession NM_022741) is another VGAM1318 host target gene. FLJ11850 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11850, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11850 BINDING SITE, designated SEQ ID:22953, to the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, also designated SEQ ID:4029.

[46693] Another function of VGAM1318 is therefore inhibition of FLJ11850 (Accession NM_022741). Accordingly, utilities of

VGAM1318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11850. FLJ20507 (Accession NM_017849) is another VGAM1318 host target gene. FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20507, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2, designated SEQ ID:19515 and SEQ ID:30223 respectively, to the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, also designated SEQ ID:4029.

[46694] Another function of VGAM1318 is therefore inhibition of FLJ20507 (Accession NM_017849). Accordingly, utilities of VGAM1318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20507. LOC126302 (Accession XM_059020) is another VGAM1318 host target gene. LOC126302 BINDING SITE1 through LOC126302 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC126302, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126302 BINDING SITE1 through LOC126302 BINDING SITE3, designated SEQ ID:36820, SEQ ID:36821 and SEQ ID:36822 respectively, to the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, also designated SEQ ID:4029.

[46695] Another function of VGAM1318 is therefore inhibition of LOC126302 (Accession XM_059020). Accordingly, utilities of VGAM1318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126302. LOC149703 (Accession XM_097719) is another VGAM1318 host target gene. LOC149703 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149703, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149703 BINDING SITE, designated SEQ ID:41063, to the nucleotide sequence of VGAM1318 RNA, herein designated VGAM RNA, also designated SEQ ID:4029.

[46696] Another function of VGAM1318 is therefore inhibition of LOC149703 (Accession XM_097719). Accordingly, utilities

of VGAM1318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149703. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1319 (VGAM1319) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46697] VGAM1319 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1319 was detected is described hereinabove with reference to Figs. 1-8.

[46698] VGAM1319 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Foot-and-mouth Disease Virus O. VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46699] VGAM1319 gene encodes a VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1319 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1319 precursor RNA is designated SEQ ID:1305, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1305 is located at position 6082 relative to the genome of Foot-and-mouth Disease Virus O.

- [46700] VGAM1319 precursor RNA folds onto itself, forming VGAM1319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46701] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1319 folded precursor RNA into VGAM1319 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1319 RNA is designated SEQ ID:4030, and

is provided hereinbelow with reference to the sequence listing part.

[46702] VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1319 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[46703] VGAM1319 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1319 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1319 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46704] The complementary binding of VGAM1319 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1319 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1319 host target RNA into VGAM1319 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46705] It is appreciated that VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1319 host target genes. The mRNA of each one of this plurality of VGAM1319 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1319 RNA, herein designated VGAM RNA, and which when bound by VGAM1319 RNA causes inhibition of translation of respective one or more VGAM1319 host target proteins.

[46706] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1319 gene, herein designated VGAM GENE, on one or more VGAM1319 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46707] It is yet further appreciated that a function of VGAM1319 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus O. Specific functions, and accordingly utilities, of VGAM1319 correlate with, and may be deduced from, the identity of the host target genes which VGAM1319 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46708] Nucleotide sequences of the VGAM1319 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1319 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1319 are further described hereinbelow with reference to Table 1.

[46709] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1319 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1319 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46710] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1319 gene, herein designated VGAM is inhibition of expression of VGAM1319 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1319 correlate with, and may be deduced from, the identity of the target genes which VGAM1319 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46711] Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM_007332) is a VGAM1319 host target gene. ANKTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKTM1 BINDING SITE, designated SEQ ID:14254, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46712] A function of VGAM1319 is therefore inhibition of Ankyrin-like with Transmembrane Domains 1 (ANKTM1, Accession NM_007332), a gene which attaches integral membrane proteins to cytoskeletal elements. Accordingly, utilities of VGAM1319 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with ANKTM1. The function of ANKTM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM644. Growth Arrest-specific 11 (GAS11, Accession NM_001481) is another VGAM1319 host target gene. GAS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS11 BINDING SITE, designated SEQ ID:7221, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46713] Another function of VGAM1319 is therefore inhibition of Growth Arrest-specific 11 (GAS11, Accession NM_001481). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS11. LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055) is another VGAM1319 host target gene. LANCL1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LANCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANCL1 BINDING SITE, designated SEQ ID:12695, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46714] Another function of VGAM1319 is therefore inhibition of LanC Lantibiotic Synthetase Component C-like 1 (bacterial) (LANCL1, Accession NM_006055), a gene which binds the C-terminus of stomatin. Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANCL1. The function of LANCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM656. Microtubule-associated Protein Tau (MAPT, Accession NM_005910) is another VGAM1319 host target gene. MAPT BINDING SITE1 through MAPT BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPT, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPT BINDING SITE1 through MAPT BINDING SITE4, designated SEQ ID:12539, SEQ ID:18827, SEQ ID:18833 and SEQ ID:18839 respectively, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46715] Another function of VGAM1319 is therefore inhibition of Microtubule-associated Protein Tau (MAPT, Accession NM_005910), a gene which Microtubule-associated protein tau; promotes microtubule assembly. Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPT. The function of MAPT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Neurexin 2 (NRXN2, Accession NM_138734) is another VGAM1319 host target gene. NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3, designated SEQ ID:28990, SEQ ID:17468 and SEQ ID:8667 respectively, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46716] Another function of VGAM1319 is therefore inhibition of Neurexin 2 (NRXN2, Accession NM_138734), a gene which may be involved in cell recognition, cell adhesion, and may mediate intracellular signaling. Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN2. The function of NRXN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.FLJ20584 (Accession NM_017891) is another VGAM1319 host target gene. FLJ20584 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20584 BINDING SITE, designated SEQ ID:19558, to the nucleotide sequence of VGAM1319 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4030.

[46717] Another function of VGAM1319 is therefore inhibition of FLJ20584 (Accession NM_017891). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20584. FLJ20699 (Accession NM_017931) is another VGAM1319 host target gene. FLJ20699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20699 BINDING SITE, designated SEQ ID:19616, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46718] Another function of VGAM1319 is therefore inhibition of FLJ20699 (Accession NM_017931). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20699. KIAA0603 (Accession NM_014832) is another VGAM1319 host target gene. KIAA0603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0603, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0603 BINDING SITE, designated SEQ ID:16830, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46719] Another function of VGAM1319 is therefore inhibition of KIAA0603 (Accession NM_014832). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0603. KIAA1399 (Accession XM_046685) is another VGAM1319 host target gene. KIAA1399 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1399 BINDING SITE, designated SEQ ID:34797, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46720] Another function of VGAM1319 is therefore inhibition of KIAA1399 (Accession XM_046685). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1399. KIAA1404 (Accession XM_030494) is another VGAM1319 host target gene. KIAA1404 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1404, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1404 BINDING SITE, designated SEQ ID:31049, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46721] Another function of VGAM1319 is therefore inhibition of KIAA1404 (Accession XM_030494). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1404. WIT-1 (Accession NM_015855) is another VGAM1319 host target gene. WIT-1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WIT-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WIT-1 BINDING SITE, designated SEQ ID:17988, to the nucleotide sequence of

VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46722] Another function of VGAM1319 is therefore inhibition of WIT-1 (Accession NM_015855). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WIT-1. LOC197342 (Accession XM_113869) is another VGAM1319 host target gene. LOC197342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197342 BINDING SITE, designated SEQ ID:42486, to the nucleotide sequence of VGAM1319 RNA, herein designated VGAM RNA, also designated SEQ ID:4030.

[46723] Another function of VGAM1319 is therefore inhibition of LOC197342 (Accession XM_113869). Accordingly, utilities of VGAM1319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197342. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1320 (VGAM1320) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46724] VGAM1320 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1320 was detected is described hereinabove with reference to Figs. 1–8.

[46725] VGAM1320 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46726] VGAM1320 gene encodes a VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1320 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1320 precursor RNA is designated SEQ ID:1306, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1306 is located at position 221058 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[46727] VGAM1320 precursor RNA folds onto itself, forming VGAM1320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46728] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1320 folded precursor RNA into VGAM1320 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1320 RNA is designated SEQ ID:4031, and is provided hereinbelow with reference to the sequence listing part.

[46729] VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1320 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1320 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46730] VGAM1320 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1320 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1320 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46731] The complementary binding of VGAM1320 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1320 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1320 host target RNA into VGAM1320 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46732] It is appreciated that VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1320 host target genes. The mRNA of each one of this plurality of VGAM1320 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1320 RNA, herein designated VGAM RNA, and which when bound by VGAM1320 RNA causes inhibition of translation of respective one or more VGAM1320 host target proteins.

[46733] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1320 gene, herein designated VGAM GENE, on one or more VGAM1320 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46734] It is yet further appreciated that a function of VGAM1320 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1320 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1320 correlate with, and may be deduced from,

the identity of the host target genes which VGAM1320 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46735] Nucleotide sequences of the VGAM1320 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1320 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1320 are further described hereinbelow with reference to Table 1.

[46736] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1320 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1320 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46737] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1320 gene, herein designated VGAM is inhibition of expression of VGAM1320 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1320 correlate with, and may be deduced from, the identity of the target genes which VGAM1320

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46738] Histidine Ammonia-lyase (HAL, Accession NM_002108) is a VGAM1320 host target gene. HAL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAL BINDING SITE, designated SEQ ID:7886, to the nucleotide sequence of VGAM1320 RNA, herein designated VGAM RNA, also designated SEQ ID:4031.

[46739] A function of VGAM1320 is therefore inhibition of Histidine Ammonia-lyase (HAL, Accession NM_002108). Accordingly, utilities of VGAM1320 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAL. TSG (Accession NM_020648) is another VGAM1320 host target gene. TSG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSG BINDING

SITE, designated SEQ ID:21809, to the nucleotide sequence of VGAM1320 RNA, herein designated VGAM RNA, also designated SEQ ID:4031.

[46740] Another function of VGAM1320 is therefore inhibition of TSG (Accession NM_020648). Accordingly, utilities of VGAM1320 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSG. BCMP1 (Accession NM_031442) is another VGAM1320 host target gene. BCMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCMP1 BINDING SITE, designated SEQ ID:25453, to the nucleotide sequence of VGAM1320 RNA, herein designated VGAM RNA, also designated SEQ ID:4031.

[46741] Another function of VGAM1320 is therefore inhibition of BCMP1 (Accession NM_031442). Accordingly, utilities of VGAM1320 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCMP1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present inven-

tion, referred to here as Viral Genomic Address Messenger 1321 (VGAM1321) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46742] VGAM1321 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1321 was detected is described hereinabove with reference to Figs. 1–8.

[46743] VGAM1321 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Melanoplus Sanguinipes Entomopoxvirus. VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46744] VGAM1321 gene encodes a VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1321 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1321 precursor RNA is designated SEQ ID:1307, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1307 is located at position 223345 relative to the genome of Melanoplus Sanguinipes Entomopoxvirus.

[46745] VGAM1321 precursor RNA folds onto itself, forming VGAM1321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46746] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1321 folded precursor RNA into VGAM1321 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1321 RNA is designated SEQ ID:4032, and is provided hereinbelow with reference to the sequence listing part.

[46747] VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1321 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1321 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46748] VGAM1321 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1321 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1321 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46749] The complementary binding of VGAM1321 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1321 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1321 host target RNA into VGAM1321 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46750] It is appreciated that VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1321 host target genes. The mRNA of each one of this plurality of VGAM1321 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1321 RNA, herein designated VGAM RNA, and which when bound by VGAM1321 RNA causes inhibition of translation of respective one or more VGAM1321 host target proteins.

[46751] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1321 gene, herein designated VGAM GENE, on one or more VGAM1321 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46752] It is yet further appreciated that a function of VGAM1321 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGAM1321 correlate with, and may be deduced from,

the identity of the host target genes which VGAM1321 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46753] Nucleotide sequences of the VGAM1321 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1321 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1321 are further described hereinbelow with reference to Table 1.

[46754] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1321 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1321 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46755] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1321 gene, herein designated VGAM is inhibition of expression of VGAM1321 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1321 correlate with, and may be deduced from, the identity of the target genes which VGAM1321

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46756] Cyclin D2 (CCND2, Accession NM_001759) is a VGAM1321 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7511, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46757] A function of VGAM1321 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the G1/S (start) transition. Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128. Chloride Channel, Calcium Activated, Family Member 2 (CLCA2, Accession NM_006536) is another

VGAM1321 host target gene. CLCA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCA2 BINDING SITE, designated SEQ ID:13289, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46758] Another function of VGAM1321 is therefore inhibition of Chloride Channel, Calcium Activated, Family Member 2 (CLCA2, Accession NM_006536), a gene which Calcium-sensitive chloride channel, is suggested to play a role in the complex pathogenesis of cystic fibrosis. Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCA2. The function of CLCA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM851. M-phase Phosphoprotein 1 (MPHOSPH1, Accession NM_016195) is another VGAM1321 host target gene. MPHOSPH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MPHOSPH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPHOSPH1 BINDING SITE, designated SEQ ID:18286, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46759] Another function of VGAM1321 is therefore inhibition of M-phase Phosphoprotein 1 (MPHOSPH1, Accession NM_016195), a gene which is Phosphorylated during M-phase and interacts with guanosine triphosphate. Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPHOSPH1. The function of MPHOSPH1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM_001716) is another VGAM1321 host target gene. BLR1 BINDING SITE1 and BLR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BLR1, corresponding to HOST TARGET binding sites such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLR1 BINDING SITE1 and BLR1 BINDING SITE2, designated SEQ ID:7446 and SEQ ID:26776 respectively, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46760] Another function of VGAM1321 is therefore inhibition of Burkitt Lymphoma Receptor 1, GTP Binding Protein (chemokine (C-X-C motif) Receptor 5) (BLR1, Accession NM_001716). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLR1. Dynein, Cytoplasmic, Light Intermediate Polypeptide 1 (DNCLI1, Accession XM_003119) is another VGAM1321 host target gene. DNCLI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNCLI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNCLI1 BINDING SITE, designated SEQ ID:29928, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46761] Another function of VGAM1321 is therefore inhibition of Dynein, Cytoplasmic, Light Intermediate Polypeptide 1 (DNCLI1, Accession XM_003119). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNCLI1. KIAA0644 (Accession NM_014817) is another VGAM1321 host target gene. KIAA0644 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0644 BINDING SITE, designated SEQ ID:16781, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46762] Another function of VGAM1321 is therefore inhibition of KIAA0644 (Accession NM_014817). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0644. M96 (Accession NM_007358) is another VGAM1321 host target gene. M96 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by M96, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M96 BINDING SITE, designated SEQ ID:14288, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46763] Another function of VGAM1321 is therefore inhibition of M96 (Accession NM_007358). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M96. MIG-6 (Accession NM_018948) is another VGAM1321 host target gene. MIG-6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIG-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG-6 BINDING SITE, designated SEQ ID:21018, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46764] Another function of VGAM1321 is therefore inhibition of MIG-6 (Accession NM_018948). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MIG-6. MRPL56 (Accession NM_032857) is another VGAM1321 host target gene. MRPL56 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL56 BINDING SITE, designated SEQ ID:26658, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46765] Another function of VGAM1321 is therefore inhibition of MRPL56 (Accession NM_032857). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL56. Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM_020841) is another VGAM1321 host target gene. OSBPL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL8 BINDING SITE, designated SEQ

ID:21901, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46766] Another function of VGAM1321 is therefore inhibition of Oxysterol Binding Protein-like 8 (OSBPL8, Accession NM_020841). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL8. LOC116068 (Accession XM_057302) is another VGAM1321 host target gene. LOC116068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116068 BINDING SITE, designated SEQ ID:36499, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46767] Another function of VGAM1321 is therefore inhibition of LOC116068 (Accession XM_057302). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116068. LOC51141 (Accession XM_043953) is an-

other VGAM1321 host target gene. LOC51141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51141 BINDING SITE, designated SEQ ID:34050, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46768] Another function of VGAM1321 is therefore inhibition of LOC51141 (Accession XM_043953). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51141. LOC92249 (Accession XM_043814) is another VGAM1321 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34017, to the nucleotide sequence of VGAM1321 RNA, herein designated VGAM RNA, also designated SEQ ID:4032.

[46769] Another function of VGAM1321 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM1321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1322 (VGAM1322) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46770] VGAM1322 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1322 was detected is described hereinabove with reference to Figs. 1-8.

[46771] VGAM1322 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus. VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46772] VGAM1322 gene encodes a VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1322 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1322 precursor RNA is designated SEQ ID:1308, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1308 is located at position 5259 relative to the genome of Garlic Latent Virus.

[46773] VGAM1322 precursor RNA folds onto itself, forming VGAM1322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46774] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1322 folded precursor RNA into VGAM1322 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1322 RNA is designated SEQ ID:4033, and is provided hereinbelow with reference to the sequence listing part.

[46775] VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1322 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[46776] VGAM1322 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1322 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1322 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[46777] The complementary binding of VGAM1322 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1322 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1322 host target RNA into VGAM1322 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46778] It is appreciated that VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1322 host target genes. The mRNA of each one of this plurality of VGAM1322 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1322 RNA, herein designated VGAM RNA, and which when bound by VGAM1322 RNA causes inhibition of translation of respective one or more VGAM1322 host target proteins.

[46779] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1322 gene, herein designated VGAM GENE, on one or more VGAM1322 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46780] It is yet further appreciated that a function of VGAM1322 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1322 correlate with, and may be deduced from, the identity of the host target genes which VGAM1322 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46781] Nucleotide sequences of the VGAM1322 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1322 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1322 are further described hereinbelow with reference to Table 1.

[46782] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1322 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1322 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[46783] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1322 gene, herein designated VGAM is inhibition of expression of VGAM1322 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1322 correlate with, and may be deduced from, the identity of the target genes which VGAM1322 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46784] Alpha-1-B Glycoprotein (A1BG, Accession NM_130786) is a VGAM1322 host target gene. A1BG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by A1BG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A1BG BINDING SITE, designated SEQ ID:28275, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46785] A function of VGAM1322 is therefore inhibition of Alpha-1-B Glycoprotein (A1BG, Accession NM_130786), a gene which a plasma protein of unknown function. Accordingly, utilities of VGAM1322 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with A1BG. The function of A1BG and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Aryl Hydrocarbon Receptor (AHR, Accession NM_001621) is another VGAM1322 host target gene. AHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AHR BINDING SITE, designated SEQ ID:7331, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46786] Another function of VGAM1322 is therefore inhibition of Aryl Hydrocarbon Receptor (AHR, Accession NM_001621), a gene which plays a role in modulating carcinogenesis through the induction of xenobiotic-metabolizing enzymes. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AHR. The function of AHR and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM368.ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM_000052) is another VGAM1322 host target gene. ATP7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP7A BINDING SITE, designated SEQ ID:5490, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46787] Another function of VGAM1322 is therefore inhibition of ATPase, Cu++ Transporting, Alpha Polypeptide (Menkes syndrome) (ATP7A, Accession NM_000052). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP7A. Calpain 10 (CAPN10, Accession NM_023084) is another VGAM1322 host target gene. CAPN10 BINDING SITE1 through CAPN10 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CAPN10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN10 BINDING SITE1 through CAPN10 BINDING SITE4, designated SEQ ID:23346, SEQ ID:23348, SEQ ID:23350 and SEQ ID:23352 respectively, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46788] Another function of VGAM1322 is therefore inhibition of Calpain 10 (CAPN10, Accession NM_023084), a gene which catalyzes limited proteolysis of substrates involved in cytoskeletal remodelling and signal transduction. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN10. The function of CAPN10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Cytochrome P450, Subfamily VIIB (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391) is another VGAM1322 host target gene. CYP8B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP8B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of CYP8B1 BINDING SITE, designated SEQ ID:10621, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46789] Another function of VGAM1322 is therefore inhibition of Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391), a gene which functions in bile acid biosynthesis. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP8B1. The function of CYP8B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366) is another VGAM1322 host target gene. DFFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DFFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DFFB BINDING SITE, designated SEQ ID:42239, to the nucleotide

sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46790] Another function of VGAM1322 is therefore inhibition of DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366), a gene which induces DNA fragmentation and chromatin condensation during apoptosis. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DFFB. The function of DFFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM_012193) is another VGAM1322 host target gene. FZD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD4 BINDING SITE, designated SEQ ID:14482, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46791] Another function of VGAM1322 is therefore inhibition of

Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM_012193), a gene which may function in cell polarity, cell fate specification and cancer; similar to frizzled receptor family, has seven transmembrane domains. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD4. The function of FZD4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM309. Male Germ Cell-associated Kinase (MAK, Accession NM_005906) is another VGAM1322 host target gene. MAK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAK BINDING SITE, designated SEQ ID:12527, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46792] Another function of VGAM1322 is therefore inhibition of Male Germ Cell-associated Kinase (MAK, Accession NM_005906), a gene which plays an important role in

spermatogenesis. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAK. The function of MAK has been established by previous studies. Male germ cell-associated kinase is one of the protein kinases that was isolated by weak cross-hybridization with the v-ros (OMIM Ref. No. 165020) protein kinase sequence (Matsushime et al., 1990). The gene encoding this kinase is expressed almost exclusively in testis, mainly in germ cells at and/or after the pachytene stage, as 66- and 60-kD proteins that form a distinct complex with cellular phosphoprotein p210. The p210 protein is sufficiently phosphorylated in vitro by the MAK gene product at serine and threonine residues. These results suggest that the MAK gene plays an important role in spermatogenesis. Using a panel of DNA samples from an interspecific cross, Taketo et al. (1994) mapped the Mak gene to mouse chromosome 13 in an area situated between 2 regions that are homologous with human chromosome 6p and chromosome 5. Taketo et al. (1994) stated that preliminary Southern analysis of DNA samples from a panel of mouse/human somatic cell hybrids showed concordant hybridization of the MAK gene and the ROS1 gene, previ-

ously mapped to 6q22

[46793] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46794] Matsushime, H.; Jinno, A.; Takagi, N.; Shibuya, M. : A novel mammalian protein kinase gene (mak) is highly expressed in testicular germ cells at and after meiosis. Molec. Cell. Biol. 10: 2261–2268, 1990. ; and

[46795] Taketo, M.; Jinno, A.; Yamaguchi, S.; Matsushime, H.; Shibuya, M.; Seldin, M. F. : Mouse Mak gene for male germ cell-associated kinase maps to chromosome 13. Genomics 19: 397–398, 1994.

[46796] Further studies establishing the function and utilities of MAK are found in John Hopkins OMIM database record ID 154235, and in cited publications numbered 2196–2197 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mediterranean Fever (MEFV, Accession NM_000243) is another VGAM1322 host target gene. MEFV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEFV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MEFV BINDING SITE, designated SEQ ID:5767, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46797] Another function of VGAM1322 is therefore inhibition of Mediterranean Fever (MEFV, Accession NM_000243). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEFV. Melan-A (MLANA, Accession NM_005511) is another VGAM1322 host target gene. MLANA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLANA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLANA BINDING SITE, designated SEQ ID:12027, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46798] Another function of VGAM1322 is therefore inhibition of Melan-A (MLANA, Accession NM_005511). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with MLANA. Membrane-spanning 4-domains, Subfamily A, Member 1 (MS4A1, Accession NM_000139) is another VGAM1322 host target gene. MS4A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MS4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MS4A1 BINDING SITE, designated SEQ ID:5634, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46799] Another function of VGAM1322 is therefore inhibition of Membrane-spanning 4-domains, Subfamily A, Member 1 (MS4A1, Accession NM_000139), a gene which may be involved in the regulation of b-cell activation and proliferation. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MS4A1. The function of MS4A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM362. Non-POU Domain Containing, Octamer-binding (NONO, Accession XM_088688) is another VGAM1322 host target gene.

NONO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NONO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NONO BINDING SITE, designated SEQ ID:39898, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46800] Another function of VGAM1322 is therefore inhibition of Non-POU Domain Containing, Octamer-binding (NONO, Accession XM_088688), a gene which is a nuclear protein which contains RNA recognition motifs. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NONO. The function of NONO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Period Homolog 2 (Drosophila) (PER2, Accession NM_022817) is another VGAM1322 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23087, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46801] Another function of VGAM1322 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Rhesus Blood Group, D Antigen (RHD, Accession NM_016124) is another VGAM1322 host target gene. RHD BINDING SITE1 and RHD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RHD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

RHD BINDING SITE1 and RHD BINDING SITE2, designated SEQ ID:18216 and SEQ ID:18336 respectively, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46802] Another function of VGAM1322 is therefore inhibition of Rhesus Blood Group, D Antigen (RHD, Accession NM_016124), a gene which Major antigen of the RH system. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHD. The function of RHD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM1322 host target gene. SEDL BINDING SITE1 and SEDL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEDL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEDL BINDING SITE1 and SEDL BINDING SITE2, designated SEQ ID:15906 and SEQ ID:32987 respectively, to the nucleotide sequence of

VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46803] Another function of VGAM1322 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190) is another VGAM1322 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9177, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46804] Another function of VGAM1322 is therefore inhibition of

TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAPBP. The function of TAPBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM122. Teratocarcinoma-derived Growth Factor 1 (TDGF1, Accession NM_003212) is another VGAM1322 host target gene. TDGF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TDGF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TDGF1 BINDING SITE, designated SEQ ID:9208, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46805] Another function of VGAM1322 is therefore inhibition of Teratocarcinoma-derived Growth Factor 1 (TDGF1, Accession NM_003212), a gene which can play a role in the determination of the epiblastic cells that subsequently give

rise to the mesoderm. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TDGF1. The function of TDGF1 has been established by previous studies. Cryptic protein is required for proper laterality development in humans. TDGF1, like CFC1, is an EGF-CFC family member and an obligate coreceptor involved in NODAL signaling, a developmental program implicated in midline, forebrain, and left-right axis development in model organisms. A mutation in the conserved CFC domain of the TDGF1 gene (187395.0001) was demonstrated by de la Cruz et al. (2002) in a patient with midline anomalies of the forebrain. The mutant protein was inactive in a zebrafish rescue assay, indicating a role for TDGF1 in human midline and forebrain development. From a teratocarcinoma cell line, Ciccodicola et al. (1989) isolated a human cDNA (referred to as CRIPTO by them) encoding a protein of 188 amino acids. The central portion of this protein shared structural similarities with the human transforming growth factor alpha (OMIM Ref. No. 190170) and epidermal growth factor (EGF; 131530). Northern blot analysis of a wide variety of tumor and normal cell lines and tissues showed that CRIPTO transcripts are detected only in un-

differentiated cells and disappear after cell differentiation induced by retinoic acid treatment.

[46806] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46807] de la Cruz, J. M.; Bamford, R. N.; Burdine, R. D.; Roessler, E.; Barkovich, A. J.; Donnai, D.; Schier, A. F.; Muenke, M. : A loss-of-function mutation in the CFC domain of TDGF1 is associated with human forebrain defects. Hum. Genet. 110: 422–428, 2002. ; and

[46808] Ciccodicola, A.; Dono, R.; Obici, S.; Simeone, A.; Zollo, M.; Persico, M. G. : Molecular characterization of a gene of the 'EGF family' expressed in undifferentiated human NTERA2 terato.

[46809] Further studies establishing the function and utilities of TDGF1 are found in John Hopkins OMIM database record ID 187395, and in cited publications numbered 593–600 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tumor Necrosis Factor Receptor Superfamily, Member 10b (TNFRSF10B, Accession NM_003842) is another VGAM1322 host target gene. TNFRSF10B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded

by TNFRSF10B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF10B BINDING SITE, designated SEQ ID:9935, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46810] Another function of VGAM1322 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 10b (TNFRSF10B, Accession NM_003842), a gene which forms complex that induces apoptosis. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF10B. The function of TNFRSF10B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM400. Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_018727) is another VGAM1322 host target gene. TRPV1 BINDING SITE1 through TRPV1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRPV1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II

or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV1 BINDING SITE1 through TRPV1 BINDING SITE4, designated SEQ ID:20810, SEQ ID:27990, SEQ ID:27998 and SEQ ID:28006 respectively, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46811] Another function of VGAM1322 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_018727), a gene which functions as a receptor for capsaicin. Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV1. The function of TRPV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM146. Zinc Finger Protein 264 (ZNF264, Accession NM_003417) is another VGAM1322 host target gene. ZNF264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ZNF264 BINDING SITE, designated SEQ ID:9453, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46812] Another function of VGAM1322 is therefore inhibition of Zinc Finger Protein 264 (ZNF264, Accession NM_003417). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF264. ARPP-19 (Accession NM_006628) is another VGAM1322 host target gene. ARPP-19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARPP-19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-19 BINDING SITE, designated SEQ ID:13418, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46813] Another function of VGAM1322 is therefore inhibition of ARPP-19 (Accession NM_006628). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-

19. ASE-1 (Accession NM_012099) is another VGAM1322 host target gene. ASE-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASE-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASE-1 BINDING SITE, designated SEQ ID:14403, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46814] Another function of VGAM1322 is therefore inhibition of ASE-1 (Accession NM_012099). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASE-1. BA108L7.2 (Accession NM_030971) is another VGAM1322 host target gene. BA108L7.2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BA108L7.2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BA108L7.2 BINDING SITE, designated SEQ ID:25235, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA,

also designated SEQ ID:4033.

[46815] Another function of VGAM1322 is therefore inhibition of BA108L7.2 (Accession NM_030971). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BA108L7.2. BICD2 (Accession XM_046863) is another VGAM1322 host target gene. BICD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BICD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BICD2 BINDING SITE, designated SEQ ID:34850, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46816] Another function of VGAM1322 is therefore inhibition of BICD2 (Accession XM_046863). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BICD2. Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456) is another VGAM1322 host target gene. C13orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

C13orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C13orf1 BINDING SITE, designated SEQ ID:21689, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46817] Another function of VGAM1322 is therefore inhibition of Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C13orf1. Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956) is another VGAM1322 host target gene. C9orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C9orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf9 BINDING SITE, designated SEQ ID:21023, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46818] Another function of VGAM1322 is therefore inhibition of

Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf9. Claudin 15 (CLDN15, Accession NM_138429) is another VGAM1322 host target gene. CLDN15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN15 BINDING SITE, designated SEQ ID:28791, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46819] Another function of VGAM1322 is therefore inhibition of Claudin 15 (CLDN15, Accession NM_138429). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN15. DCOHM (Accession NM_032151) is another VGAM1322 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25841, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46820] Another function of VGAM1322 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. FLJ10232 (Accession NM_018033) is another VGAM1322 host target gene. FLJ10232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10232 BINDING SITE, designated SEQ ID:19772, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46821] Another function of VGAM1322 is therefore inhibition of FLJ10232 (Accession NM_018033). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10232. FLJ10535 (Accession NM_018129) is another VGAM1322 host target gene. FLJ10535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10535 BINDING SITE, designated SEQ ID:19916, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46822] Another function of VGAM1322 is therefore inhibition of FLJ10535 (Accession NM_018129). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10535. FLJ10922 (Accession NM_018273) is another VGAM1322 host target gene. FLJ10922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10922 BINDING SITE, designated SEQ ID:20253, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM

RNA, also designated SEQ ID:4033.

[46823] Another function of VGAM1322 is therefore inhibition of FLJ10922 (Accession NM_018273). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10922. FLJ12572 (Accession NM_022905) is another VGAM1322 host target gene. FLJ12572 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23196, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46824] Another function of VGAM1322 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. FLJ14642 (Accession NM_032818) is another VGAM1322 host target gene. FLJ14642 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14642, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14642 BINDING SITE, designated SEQ ID:26593, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46825] Another function of VGAM1322 is therefore inhibition of FLJ14642 (Accession NM_032818). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14642. FLJ20136 (Accession NM_017684) is another VGAM1322 host target gene. FLJ20136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20136 BINDING SITE, designated SEQ ID:19227, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46826] Another function of VGAM1322 is therefore inhibition of FLJ20136 (Accession NM_017684). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20136. FLJ20344 (Accession NM_017776) is another VGAM1322 host target gene. FLJ20344 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20344, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20344 BINDING SITE, designated SEQ ID:19403, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46827] Another function of VGAM1322 is therefore inhibition of FLJ20344 (Accession NM_017776). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20344. FLJ20452 (Accession NM_017828) is another VGAM1322 host target gene. FLJ20452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20452 BINDING SITE, designated SEQ ID:19490, to the nucleotide

sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46828] Another function of VGAM1322 is therefore inhibition of FLJ20452 (Accession NM_017828). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20452. FLJ23356 (Accession NM_032237) is another VGAM1322 host target gene. FLJ23356 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23356, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23356 BINDING SITE, designated SEQ ID:25957, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46829] Another function of VGAM1322 is therefore inhibition of FLJ23356 (Accession NM_032237). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23356. FLJ23563 (Accession XM_041701) is another VGAM1322 host target gene. FLJ23563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ23563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23563 BINDING SITE, designated SEQ ID:33559, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46830] Another function of VGAM1322 is therefore inhibition of FLJ23563 (Accession XM_041701). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23563. FLJ30532 (Accession NM_144724) is another VGAM1322 host target gene. FLJ30532 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30532 BINDING SITE, designated SEQ ID:29547, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46831] Another function of VGAM1322 is therefore inhibition of FLJ30532 (Accession NM_144724). Accordingly, utilities of

VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30532. FLJ31153 (Accession NM_144600) is another VGAM1322 host target gene. FLJ31153 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ31153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31153 BINDING SITE, designated SEQ ID:29412, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46832] Another function of VGAM1322 is therefore inhibition of FLJ31153 (Accession NM_144600). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31153. GRWD (Accession NM_031485) is another VGAM1322 host target gene. GRWD BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GRWD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRWD BINDING SITE,

designated SEQ ID:25576, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46833] Another function of VGAM1322 is therefore inhibition of GRWD (Accession NM_031485). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRWD. H2AV (Accession NM_138635) is another VGAM1322 host target gene. H2AV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H2AV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AV BINDING SITE, designated SEQ ID:28908, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46834] Another function of VGAM1322 is therefore inhibition of H2AV (Accession NM_138635). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AV. HCA4 (Accession XM_085287) is another VGAM1322 host target gene. HCA4 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38020, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46835] Another function of VGAM1322 is therefore inhibition of HCA4 (Accession XM_085287). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA4. KIAA0022 (Accession NM_014880) is another VGAM1322 host target gene. KIAA0022 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0022 BINDING SITE, designated SEQ ID:17025, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46836] Another function of VGAM1322 is therefore inhibition of

KIAA0022 (Accession NM_014880). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0022. KIAA0186 (Accession NM_021067) is another VGAM1322 host target gene. KIAA0186 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0186 BINDING SITE, designated SEQ ID:22036, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46837] Another function of VGAM1322 is therefore inhibition of KIAA0186 (Accession NM_021067). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0186. KIAA0453 (Accession XM_044546) is another VGAM1322 host target gene. KIAA0453 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0453 BINDING SITE, designated SEQ ID:34228, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46838] Another function of VGAM1322 is therefore inhibition of KIAA0453 (Accession XM_044546). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0453. KIAA0475 (Accession NM_014864) is another VGAM1322 host target gene. KIAA0475 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0475 BINDING SITE, designated SEQ ID:16947, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46839] Another function of VGAM1322 is therefore inhibition of KIAA0475 (Accession NM_014864). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0475. KIAA0514 (Accession NM_014696) is another

VGAM1322 host target gene. KIAA0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16204, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46840] Another function of VGAM1322 is therefore inhibition of KIAA0514 (Accession NM_014696). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. KIAA0557 (Accession XM_085507) is another VGAM1322 host target gene. KIAA0557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0557 BINDING SITE, designated SEQ ID:38203, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46841] Another function of VGAM1322 is therefore inhibition of KIAA0557 (Accession XM_085507). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0557. KIAA0599 (Accession XM_085127) is another VGAM1322 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37854, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46842] Another function of VGAM1322 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA0945 (Accession NM_014952) is another VGAM1322 host target gene. KIAA0945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0945, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0945 BINDING SITE, designated SEQ ID:17290, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46843] Another function of VGAM1322 is therefore inhibition of KIAA0945 (Accession NM_014952). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0945. KIAA1028 (Accession XM_166324) is another VGAM1322 host target gene. KIAA1028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1028 BINDING SITE, designated SEQ ID:44154, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46844] Another function of VGAM1322 is therefore inhibition of KIAA1028 (Accession XM_166324). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1028. KIAA1040 (Accession XM_051091) is another VGAM1322 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1040 BINDING SITE, designated SEQ ID:35739, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46845] Another function of VGAM1322 is therefore inhibition of KIAA1040 (Accession XM_051091). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. KIAA1198 (Accession XM_032674) is another VGAM1322 host target gene. KIAA1198 BINDING SITE1 and KIAA1198 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1198, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE1 and KIAA1198 BINDING SITE2, designated SEQ ID:31703 and SEQ

ID:31704 respectively, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46846] Another function of VGAM1322 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1497 (Accession XM_041431) is another VGAM1322 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33524, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46847] Another function of VGAM1322 is therefore inhibition of KIAA1497 (Accession XM_041431). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1497. KIAA1582 (Accession XM_037262) is another VGAM1322 host target gene. KIAA1582 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32581, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46848] Another function of VGAM1322 is therefore inhibition of KIAA1582 (Accession XM_037262). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. KIAA1829 (Accession XM_030378) is another VGAM1322 host target gene. KIAA1829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1829 BINDING SITE, designated SEQ ID:31028, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46849] Another function of VGAM1322 is therefore inhibition of

KIAA1829 (Accession XM_030378). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1829. KIAA1915 (Accession XM_055481) is another VGAM1322 host target gene. KIAA1915 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1915 BINDING SITE, designated SEQ ID:36268, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46850] Another function of VGAM1322 is therefore inhibition of KIAA1915 (Accession XM_055481). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1915. KIAA1918 (Accession XM_054951) is another VGAM1322 host target gene. KIAA1918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1918 BINDING SITE, designated SEQ ID:36212, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46851] Another function of VGAM1322 is therefore inhibition of KIAA1918 (Accession XM_054951). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1918. KIAA1971 (Accession XM_058720) is another VGAM1322 host target gene. KIAA1971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1971 BINDING SITE, designated SEQ ID:36728, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46852] Another function of VGAM1322 is therefore inhibition of KIAA1971 (Accession XM_058720). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1971. KIAA1987 (Accession XM_113870) is another

VGAM1322 host target gene. KIAA1987 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1987 BINDING SITE, designated SEQ ID:42494, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46853] Another function of VGAM1322 is therefore inhibition of KIAA1987 (Accession XM_113870). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1987. Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277) is another VGAM1322 host target gene. KLK7 BINDING SITE1 and KLK7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK7 BINDING SITE1 and KLK7 BINDING SITE2, designated SEQ ID:29273 and SEQ ID:11476 respectively, to the nucleotide se-

quence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46854] Another function of VGAM1322 is therefore inhibition of Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK7. MGC3771 (Accession NM_030970) is another VGAM1322 host target gene. MGC3771 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC3771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3771 BINDING SITE, designated SEQ ID:25233, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46855] Another function of VGAM1322 is therefore inhibition of MGC3771 (Accession NM_030970). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3771. MGC4638 (Accession NM_031479) is another VGAM1322 host target gene. MGC4638 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4638 BINDING SITE, designated SEQ ID:25557, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46856] Another function of VGAM1322 is therefore inhibition of MGC4638 (Accession NM_031479). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4638. Makorin, Ring Finger Protein, 4 (MKRN4, Accession NM_030757) is another VGAM1322 host target gene. MKRN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKRN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN4 BINDING SITE, designated SEQ ID:25041, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46857] Another function of VGAM1322 is therefore inhibition of Makorin, Ring Finger Protein, 4 (MKRN4, Accession NM_030757). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN4. Mitochondrial Ribosomal Protein L44 (MRPL44, Accession NM_022915) is another VGAM1322 host target gene. MRPL44 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL44 BINDING SITE, designated SEQ ID:23226, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46858] Another function of VGAM1322 is therefore inhibition of Mitochondrial Ribosomal Protein L44 (MRPL44, Accession NM_022915). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL44. Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM_015084) is another VGAM1322 host target gene. MRPS27 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by MRPS27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS27 BINDING SITE, designated SEQ ID:17473, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46859] Another function of VGAM1322 is therefore inhibition of Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM_015084). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS27.

p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168) is another VGAM1322 host target gene. PAK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK6 BINDING SITE, designated SEQ ID:21390, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46860] Another function of VGAM1322 is therefore inhibition of

p21(CDKN1A)–activated Kinase 6 (PAK6, Accession NM_020168). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK6. PRO0365 (Accession NM_014126) is another VGAM1322 host target gene. PRO0365 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO0365, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0365 BINDING SITE, designated SEQ ID:15385, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46861] Another function of VGAM1322 is therefore inhibition of PRO0365 (Accession NM_014126). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0365. Solute Carrier Family 2 (facilitated glucose transporter), Member 10 (SLC2A10, Accession NM_030777) is another VGAM1322 host target gene. SLC2A10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

SLC2A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A10 BINDING SITE, designated SEQ ID:25062, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46862] Another function of VGAM1322 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 10 (SLC2A10, Accession NM_030777). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A10. SSH2 (Accession XM_030846) is another VGAM1322 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31177, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46863] Another function of VGAM1322 is therefore inhibition of

SSH2 (Accession XM_030846). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. TU12B1-TY (Accession NM_016575) is another VGAM1322 host target gene. TU12B1-TY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU12B1-TY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU12B1-TY BINDING SITE, designated SEQ ID:18643, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46864] Another function of VGAM1322 is therefore inhibition of TU12B1-TY (Accession NM_016575). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TU12B1-TY. LOC115704 (Accession XM_056533) is another VGAM1322 host target gene. LOC115704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC115704 BINDING SITE, designated SEQ ID:36401, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46865] Another function of VGAM1322 is therefore inhibition of LOC115704 (Accession XM_056533). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115704. LOC116236 (Accession XM_057674) is another VGAM1322 host target gene. LOC116236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116236 BINDING SITE, designated SEQ ID:36544, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46866] Another function of VGAM1322 is therefore inhibition of LOC116236 (Accession XM_057674). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116236. LOC120526 (Accession XM_058475) is an-

other VGAM1322 host target gene. LOC120526 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120526, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120526 BINDING SITE, designated SEQ ID:36623, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46867] Another function of VGAM1322 is therefore inhibition of LOC120526 (Accession XM_058475). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120526. LOC121506 (Accession XM_058570) is another VGAM1322 host target gene. LOC121506 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121506 BINDING SITE, designated SEQ ID:36667, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46868] Another function of VGAM1322 is therefore inhibition of LOC121506 (Accession XM_058570). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121506. LOC128387 (Accession XM_059243) is another VGAM1322 host target gene. LOC128387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128387 BINDING SITE, designated SEQ ID:36928, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46869] Another function of VGAM1322 is therefore inhibition of LOC128387 (Accession XM_059243). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128387. LOC132625 (Accession XM_067946) is another VGAM1322 host target gene. LOC132625 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC132625, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132625 BINDING SITE, designated SEQ ID:37372, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46870] Another function of VGAM1322 is therefore inhibition of LOC132625 (Accession XM_067946). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132625. LOC135763 (Accession NM_138572) is another VGAM1322 host target gene. LOC135763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135763 BINDING SITE, designated SEQ ID:28880, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46871] Another function of VGAM1322 is therefore inhibition of LOC135763 (Accession NM_138572). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC135763. LOC143187 (Accession NM_145206) is another VGAM1322 host target gene. LOC143187 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143187 BINDING SITE, designated SEQ ID:29743, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46872] Another function of VGAM1322 is therefore inhibition of LOC143187 (Accession NM_145206). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143187. LOC145226 (Accession XM_085058) is another VGAM1322 host target gene. LOC145226 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145226 BINDING SITE, designated SEQ ID:37810, to the nucleotide sequence of VGAM1322 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4033.

[46873] Another function of VGAM1322 is therefore inhibition of LOC145226 (Accession XM_085058). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145226. LOC145955 (Accession XM_096912) is another VGAM1322 host target gene. LOC145955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145955 BINDING SITE, designated SEQ ID:40643, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46874] Another function of VGAM1322 is therefore inhibition of LOC145955 (Accession XM_096912). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145955. LOC146455 (Accession XM_085471) is another VGAM1322 host target gene. LOC146455 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146455, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146455 BINDING SITE, designated SEQ ID:38156, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46875] Another function of VGAM1322 is therefore inhibition of LOC146455 (Accession XM_085471). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146455. LOC146909 (Accession XM_085634) is another VGAM1322 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38264, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46876] Another function of VGAM1322 is therefore inhibition of LOC146909 (Accession XM_085634). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC146909. LOC147429 (Accession XM_085793) is another VGAM1322 host target gene. LOC147429 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147429 BINDING SITE, designated SEQ ID:38336, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46877] Another function of VGAM1322 is therefore inhibition of LOC147429 (Accession XM_085793). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147429. LOC149117 (Accession XM_097587) is another VGAM1322 host target gene. LOC149117 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149117 BINDING SITE, designated SEQ ID:40953, to

the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46878] Another function of VGAM1322 is therefore inhibition of LOC149117 (Accession XM_097587). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149117. LOC149461 (Accession XM_086547) is another VGAM1322 host target gene. LOC149461 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149461 BINDING SITE, designated SEQ ID:38760, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46879] Another function of VGAM1322 is therefore inhibition of LOC149461 (Accession XM_086547). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149461. LOC149836 (Accession XM_086685) is another VGAM1322 host target gene. LOC149836 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC149836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149836 BINDING SITE, designated SEQ ID:38824, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46880] Another function of VGAM1322 is therefore inhibition of LOC149836 (Accession XM_086685). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149836. LOC150054 (Accession XM_097797) is another VGAM1322 host target gene. LOC150054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150054 BINDING SITE, designated SEQ ID:41124, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46881] Another function of VGAM1322 is therefore inhibition of LOC150054 (Accession XM_097797). Accordingly, utilities

of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150054. LOC150960 (Accession XM_087059) is another VGAM1322 host target gene. LOC150960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150960 BINDING SITE, designated SEQ ID:39029, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46882] Another function of VGAM1322 is therefore inhibition of LOC150960 (Accession XM_087059). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150960. LOC152925 (Accession XM_087559) is another VGAM1322 host target gene. LOC152925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC152925 BINDING SITE, designated SEQ ID:39329, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46883] Another function of VGAM1322 is therefore inhibition of LOC152925 (Accession XM_087559). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152925. LOC154739 (Accession XM_098602) is another VGAM1322 host target gene. LOC154739 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154739 BINDING SITE, designated SEQ ID:41715, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46884] Another function of VGAM1322 is therefore inhibition of LOC154739 (Accession XM_098602). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154739. LOC157798 (Accession XM_098827) is another VGAM1322 host target gene. LOC157798 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157798 BINDING SITE, designated SEQ ID:41846, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46885] Another function of VGAM1322 is therefore inhibition of LOC157798 (Accession XM_098827). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157798. LOC158237 (Accession XM_017584) is another VGAM1322 host target gene. LOC158237 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158237 BINDING SITE, designated SEQ ID:30326, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46886] Another function of VGAM1322 is therefore inhibition of

LOC158237 (Accession XM_017584). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158237. LOC165229 (Accession XM_092464) is another VGAM1322 host target gene. LOC165229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165229 BINDING SITE, designated SEQ ID:40124, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46887] Another function of VGAM1322 is therefore inhibition of LOC165229 (Accession XM_092464). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165229. LOC170082 (Accession XM_093092) is another VGAM1322 host target gene. LOC170082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC170082 BINDING SITE, designated SEQ ID:40168, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46888] Another function of VGAM1322 is therefore inhibition of LOC170082 (Accession XM_093092). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170082. LOC196264 (Accession XM_113683) is another VGAM1322 host target gene. LOC196264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196264 BINDING SITE, designated SEQ ID:42333, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46889] Another function of VGAM1322 is therefore inhibition of LOC196264 (Accession XM_113683). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196264. LOC200169 (Accession XM_117200) is an-

other VGAM1322 host target gene. LOC200169 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200169 BINDING SITE, designated SEQ ID:43283, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46890] Another function of VGAM1322 is therefore inhibition of LOC200169 (Accession XM_117200). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200169. LOC200314 (Accession XM_117225) is another VGAM1322 host target gene. LOC200314 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200314, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200314 BINDING SITE, designated SEQ ID:43292, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46891] Another function of VGAM1322 is therefore inhibition of LOC200314 (Accession XM_117225). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200314. LOC200339 (Accession XM_117226) is another VGAM1322 host target gene. LOC200339 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200339, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200339 BINDING SITE, designated SEQ ID:43296, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46892] Another function of VGAM1322 is therefore inhibition of LOC200339 (Accession XM_117226). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200339. LOC200860 (Accession XM_117289) is another VGAM1322 host target gene. LOC200860 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200860 BINDING SITE, designated SEQ ID:43352, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46893] Another function of VGAM1322 is therefore inhibition of LOC200860 (Accession XM_117289). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC200860. LOC201292 (Accession XM_113949) is another VGAM1322 host target gene. LOC201292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201292 BINDING SITE, designated SEQ ID:42562, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46894] Another function of VGAM1322 is therefore inhibition of LOC201292 (Accession XM_113949). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201292. LOC201294 (Accession XM_113950) is another VGAM1322 host target gene. LOC201294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201294 BINDING SITE, designated SEQ ID:42565, to the nucleotide sequence of VGAM1322 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4033.

[46895] Another function of VGAM1322 is therefore inhibition of LOC201294 (Accession XM_113950). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201294. LOC203276 (Accession XM_117523) is another VGAM1322 host target gene. LOC203276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203276 BINDING SITE, designated SEQ ID:43482, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46896] Another function of VGAM1322 is therefore inhibition of LOC203276 (Accession XM_117523). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203276. LOC203305 (Accession XM_117529) is another VGAM1322 host target gene. LOC203305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203305, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203305 BINDING SITE, designated SEQ ID:43506, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46897] Another function of VGAM1322 is therefore inhibition of LOC203305 (Accession XM_117529). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203305. LOC220662 (Accession XM_165978) is another VGAM1322 host target gene. LOC220662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220662 BINDING SITE, designated SEQ ID:43821, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46898] Another function of VGAM1322 is therefore inhibition of LOC220662 (Accession XM_165978). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC220662. LOC222070 (Accession XM_168433) is another VGAM1322 host target gene. LOC222070 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC222070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222070 BINDING SITE, designated SEQ ID:45177, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46899] Another function of VGAM1322 is therefore inhibition of LOC222070 (Accession XM_168433). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222070. LOC254243 (Accession XM_173233) is another VGAM1322 host target gene. LOC254243 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC254243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254243 BINDING SITE, designated SEQ ID:46508, to

the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46900] Another function of VGAM1322 is therefore inhibition of LOC254243 (Accession XM_173233). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254243. LOC51193 (Accession NM_016331) is another VGAM1322 host target gene. LOC51193 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51193 BINDING SITE, designated SEQ ID:18453, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46901] Another function of VGAM1322 is therefore inhibition of LOC51193 (Accession NM_016331). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51193. LOC51200 (Accession NM_016352) is another VGAM1322 host target gene. LOC51200 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC51200, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51200 BINDING SITE, designated SEQ ID:18480, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46902] Another function of VGAM1322 is therefore inhibition of LOC51200 (Accession NM_016352). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51200. LOC89932 (Accession XM_027341) is another VGAM1322 host target gene. LOC89932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89932 BINDING SITE, designated SEQ ID:30487, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46903] Another function of VGAM1322 is therefore inhibition of LOC89932 (Accession XM_027341). Accordingly, utilities

of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89932. LOC90038 (Accession XM_028305) is another VGAM1322 host target gene. LOC90038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90038 BINDING SITE, designated SEQ ID:30645, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46904] Another function of VGAM1322 is therefore inhibition of LOC90038 (Accession XM_028305). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90038. LOC90371 (Accession XM_031261) is another VGAM1322 host target gene. LOC90371 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90371 BINDING SITE, designated SEQ ID:31319, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46905] Another function of VGAM1322 is therefore inhibition of LOC90371 (Accession XM_031261). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90371. LOC90408 (Accession XM_031517) is another VGAM1322 host target gene. LOC90408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90408 BINDING SITE, designated SEQ ID:31394, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46906] Another function of VGAM1322 is therefore inhibition of LOC90408 (Accession XM_031517). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90408. LOC92249 (Accession XM_043814) is another VGAM1322 host target gene. LOC92249 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34023, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46907] Another function of VGAM1322 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. LOC92283 (Accession XM_044049) is another VGAM1322 host target gene. LOC92283 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92283 BINDING SITE, designated SEQ ID:34091, to the nucleotide sequence of VGAM1322 RNA, herein designated VGAM RNA, also designated SEQ ID:4033.

[46908] Another function of VGAM1322 is therefore inhibition of

LOC92283 (Accession XM_044049). Accordingly, utilities of VGAM1322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92283. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1323 (VGAM1323) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46909] VGAM1323 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1323 was detected is described hereinabove with reference to Figs. 1-8.

[46910] VGAM1323 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus. VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46911] VGAM1323 gene encodes a VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1323 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1323 precursor RNA is designated SEQ ID:1309, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1309 is located at position 5155 relative to the genome of Garlic Latent Virus.

- [46912] VGAM1323 precursor RNA folds onto itself, forming VGAM1323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [46913] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1323 folded precursor RNA into VGAM1323 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide se-

quence of VGAM1323 RNA is designated SEQ ID:4034, and is provided hereinbelow with reference to the sequence listing part.

[46914] VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1323 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[46915] VGAM1323 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1323 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1323 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[46916] The complementary binding of VGAM1323 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1323 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1323 host target RNA into VGAM1323 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46917] It is appreciated that VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1323 host target genes. The mRNA of each one of this plurality of VGAM1323 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1323 RNA, herein designated VGAM RNA, and which when bound by VGAM1323 RNA causes inhibition of translation of respective one or more VGAM1323 host target proteins.

[46918] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1323 gene, herein designated VGAM GENE, on one or more VGAM1323 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46919] It is yet further appreciated that a function of VGAM1323

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1323 correlate with, and may be deduced from, the identity of the host target genes which VGAM1323 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46920] Nucleotide sequences of the VGAM1323 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1323 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1323 are further described hereinbelow with reference to Table 1.

[46921] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1323 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1323 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46922] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1323 gene, herein designated VGAM is inhibition of expression of VGAM1323 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1323 correlate with, and may be deduced from, the identity of the target genes which VGAM1323 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46923] Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM_130442) is a VGAM1323 host target gene. ELMO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELMO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELMO1 BINDING SITE, designated SEQ ID:28201, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46924] A function of VGAM1323 is therefore inhibition of Engulfment and Cell Motility 1 (ced-12 homolog, *C. elegans*) (ELMO1, Accession NM_130442). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ELMO1. Formin 2 (FMN2, Accession XM_086525) is another VGAM1323 host target gene. FMN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FMN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMN2 BINDING SITE, designated SEQ ID:38742, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46925] Another function of VGAM1323 is therefore inhibition of Formin 2 (FMN2, Accession XM_086525). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMN2. Glycogen Synthase 1 (muscle) (GYS1, Accession XM_114024) is another VGAM1323 host target gene. GYS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GYS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GYS1 BINDING SITE, designated SEQ ID:42625,

to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46926] Another function of VGAM1323 is therefore inhibition of Glycogen Synthase 1 (muscle) (GYS1, Accession XM_114024), a gene which transfers the glycosyl residue from udp-glc to the nonreducing end of alpha-1,4-glucan. Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GYS1. The function of GYS1 has been established by previous studies. To examine whether defective muscle GYS1 expression is associated with impaired glycogen synthesis in type 2 diabetes and whether the defect is inherited or acquired, Huang et al. (2000) measured GYS1 gene expression and enzyme activity in muscle biopsies taken before and after an insulin clamp in 12 monozygotic twin pairs discordant for type 2 diabetes and in 12 matched control subjects. The effect of insulin on GYS1 fractional activity, when expressed as the increment over the basal values, was significantly impaired in diabetic ($15.7 \pm 3.3\%$; P less than 0.01), but not in nondiabetic ($23.7 \pm 1.8\%$; $P = \text{NS}$) twins compared with that in control subjects ($28.1 \pm 2.3\%$). Insulin increased GYS1 mRNA expression in control subjects

(from 0.14 \pm 0.02 to 1.74 \pm 0.10 relative units; P less than 0.01) and in nondiabetic (from 0.24 \pm 0.05 to 1.81 \pm 0.16 relative units; P less than 0.01) and diabetic (from 0.20 \pm 0.07 to 1.08 \pm 0.14 relative units; P less than 0.01) twins. The effect of insulin on GYS1 expression was, however, significantly reduced in the diabetic (P less than 0.003), but not in the nondiabetic, twins, compared with that in control subjects. The postclamp GYS1 mRNA levels correlated strongly with the hemoglobin A1c levels ($r = -0.61$; P less than 0.001). The authors concluded that insulin stimulates GYS1 mRNA expression and that impaired stimulation of GYS1 gene expression by insulin in patients with type 2 diabetes is acquired and most likely is secondary to chronic hyperglycemia. Inbred mouse strains fed on a diabetogenic diet (high in fat and sucrose) differ in their propensities to develop features analogous to type 2 diabetes mellitus. To define chromosomal locations that control these characteristics, Seldin et al. (1994) studied recombinant inbred strains from diabetes-prone C57BL/6J and diabetes-resistant A/J strains. Hyperglycemia correlated with the marker D7Mit25 on mouse chromosome 7. This putative susceptibility locus is consistent with that of the glycogen synthase gene, which was implicated by

Groop et al. (1993) in the pathogenesis of type 2 diabetes in the human. Seldin et al. (1994) found that fractional glycogen synthase activity in isolated muscle was significantly lower in normal B/6J diabetes-prone mice than in normal diabetes-resistant A/J mice, a finding similar to that reported in relatives of human patients with type 2 diabetes.

[46927] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46928] Huang, X.; Vaag, A.; Hansson, M.; Weng, J.; Laurila, E.; Groop, L. : Impaired insulin-stimulated expression of the glycogen synthase gene in skeletal muscle of type 2 diabetic patients is acquired rather than inherited. J. Clin. Endocr. Metab. 85: 1584–1590, 2000. ; and

[46929] Seldin, M. F.; Mott, D.; Bhat, D.; Petro, A.; Kuhn, C. M.; Kingsmore, S. F.; Bogardus, C.; Opara, E.; Feinglos, M. N.; Surwit, R. S. : Glycogen synthase: a putative locus for diet-induc.

[46930] Further studies establishing the function and utilities of GYS1 are found in John Hopkins OMIM database record ID 138570, and in cited publications numbered 11617–11623 listed in the bibliography section hereinbe–

low, which are also hereby incorporated by reference. Single-minded Homolog 1 (Drosophila) (SIM1, Accession NM_005068) is another VGAM1323 host target gene. SIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM1 BINDING SITE, designated SEQ ID:11508, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46931] Another function of VGAM1323 is therefore inhibition of Single-minded Homolog 1 (Drosophila) (SIM1, Accession NM_005068), a gene which may have pleiotropic effects during embryogenesis and in the adult. Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM1. The function of SIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM665.FLJ11383 (Accession NM_024938) is another VGAM1323 host target gene. FLJ11383 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by FLJ11383, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11383 BINDING SITE, designated SEQ ID:24479, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46932] Another function of VGAM1323 is therefore inhibition of FLJ11383 (Accession NM_024938). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11383. KIAA0268 (Accession XM_046126) is another VGAM1323 host target gene. KIAA0268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0268 BINDING SITE, designated SEQ ID:34686, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46933] Another function of VGAM1323 is therefore inhibition of KIAA0268 (Accession XM_046126). Accordingly, utilities

of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0268. KIAA0416 (Accession NM_015564) is another VGAM1323 host target gene. KIAA0416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0416 BINDING SITE, designated SEQ ID:17838, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46934] Another function of VGAM1323 is therefore inhibition of KIAA0416 (Accession NM_015564). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0416. KIAA0836 (Accession XM_035390) is another VGAM1323 host target gene. KIAA0836 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0836 BINDING SITE, designated SEQ ID:32244, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46935] Another function of VGAM1323 is therefore inhibition of KIAA0836 (Accession XM_035390). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. KIAA0884 (Accession XM_046660) is another VGAM1323 host target gene. KIAA0884 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0884 BINDING SITE, designated SEQ ID:34774, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46936] Another function of VGAM1323 is therefore inhibition of KIAA0884 (Accession XM_046660). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0884. SMOC1 (Accession NM_022137) is another VGAM1323 host target gene. SMOC1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMOC1 BINDING SITE, designated SEQ ID:22699, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46937] Another function of VGAM1323 is therefore inhibition of SMOC1 (Accession NM_022137). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMOC1. LOC115399 (Accession XM_055874) is another VGAM1323 host target gene. LOC115399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115399 BINDING SITE, designated SEQ ID:36343, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46938] Another function of VGAM1323 is therefore inhibition of

LOC115399 (Accession XM_055874). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115399. LOC116236 (Accession XM_057674) is another VGAM1323 host target gene. LOC116236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116236 BINDING SITE, designated SEQ ID:36543, to the nucleotide sequence of VGAM1323 RNA, herein designated VGAM RNA, also designated SEQ ID:4034.

[46939] Another function of VGAM1323 is therefore inhibition of LOC116236 (Accession XM_057674). Accordingly, utilities of VGAM1323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116236. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1324 (VGAM1324) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[46940] VGAM1324 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1324 was detected is described hereinabove with reference to Figs. 1–8.

[46941] VGAM1324 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus. VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46942] VGAM1324 gene encodes a VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1324 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1324 precursor RNA is designated SEQ ID:1310, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1310 is located at position 4855 relative to the genome of Garlic Latent Virus.

[46943] VGAM1324 precursor RNA folds onto itself, forming VGAM1324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[46944] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1324 folded precursor RNA into VGAM1324 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1324 RNA is designated SEQ ID:4035, and is provided hereinbelow with reference to the sequence listing part.

[46945] VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1324 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[46946] VGAM1324 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1324 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1324 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[46947] The complementary binding of VGAM1324 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1324 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1324 host target RNA into VGAM1324 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[46948] It is appreciated that VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1324 host target genes. The mRNA of each one of this plurality of VGAM1324 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1324 RNA, herein designated VGAM RNA, and which when bound by VGAM1324 RNA causes inhibition of translation of respective one or more VGAM1324 host target proteins.

[46949] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1324 gene, herein designated VGAM GENE, on one

or more VGAM1324 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[46950] It is yet further appreciated that a function of VGAM1324 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1324 correlate with, and may be deduced from, the identity of the host target genes which VGAM1324 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[46951] Nucleotide sequences of the VGAM1324 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1324 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1324 are further described hereinbelow with reference to Table 1.

[46952] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1324 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1324 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[46953] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1324 gene, herein designated VGAM is inhibition of expression of VGAM1324 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1324 correlate with, and may be deduced from, the identity of the target genes which VGAM1324 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[46954] Chemokine (C-C motif) Receptor 9 (CCR9, Accession

NM_006641) is a VGAM1324 host target gene. CCR9 BINDING SITE1 and CCR9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR9 BINDING SITE1 and CCR9 BINDING SITE2, designated SEQ ID:13433 and SEQ ID:25250 respectively, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46955] A function of VGAM1324 is therefore inhibition of Chemokine (C-C motif) Receptor 9 (CCR9, Accession NM_006641), a gene which binds beta-chemokine family and subsequently transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR9. The function of CCR9 has been established by previous studies. Chemokines are small peptides involved in the chemotaxis and activation of leukocytes in response to inflammation, tissue damage, or infection. Chemokine receptors belong to the superfamily of G protein-coupled

receptors. See CMKBR1 (OMIM Ref. No. 601159) for background. Nibbs et al. (1997) stated that they had previously identified the mouse cysteine–cysteine (C–C) chemokine receptor D6. To identify the human homolog of D6, they performed PCR on human genomic DNA using primers based on the sequence of the mouse D6 gene. The human D6 gene encodes a predicted 384–amino acid protein that contains the characteristic 7 transmembrane domains and 4 conserved cysteine residues of chemokine receptors. The human and mouse D6 proteins share 71% amino acid identity. By Northern blot analysis, human D6 is expressed as approximately 4– and 6–kb transcripts in several tissues, with the highest expression in placenta. Although human D6 binds with relatively high–affinity to the majority of members of the beta–chemokine family (for example, MCP2; 602283), Nibbs et al. (1997) were unable to demonstrate any signaling following the ligand binding. Therefore, the International Union of Pharmacology (OMIM Ref. No. IUPHAR) proposed that the human D6 receptor be designated ccr9, with the lower cases indicating that receptor function has not been demonstrated. Bonini et al. (1997) cloned a cDNA encoding CMKBR9, which they called CCR10 because it is homologous to rat

'Ccr10-related receptor' (Ccr10rR). The CMKBR9 and rat Ccr10rR proteins have 72% amino acid identity. By PCR of a radiation hybrid panel, Bonini et al. (1997) mapped the CMKBR9 (CCBP2) gene to 3p21.32-p21.31, a region containing other C-C chemokine receptor genes such as CMKBR1, CMKBR2 (OMIM Ref. No. 601267), CMKBR3 (OMIM Ref. No. 601268), and CMKBR5 (OMIM Ref. No. 601373). By radiation hybrid analysis and organization of BAC contigs by FISH on combed genomic DNA, Maho et al. (1999) localized the CCBP2 gene within the CCR cluster at 3p21.3.

[46956] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[46957] Nibbs, R. J. B.; Wylie, S. M.; Yang, J.; Landau, N. R.; Graham, G. J. : Cloning and characterization of a novel promiscuous human beta-chemokine receptor D6. *J. Biol. Chem.* 272: 32078-32083, 1997. ; and

[46958] Bonini, J. A.; Martin, S. K.; Dralyuk, F.; Roe, M. W.; Philipson, L. H.; Steiner, D. F. : Cloning, expression, and chromosomal mapping of a novel human CC-chemokine receptor (CCR10) that.

[46959] Further studies establishing the function and utilities of

CCR9 are found in John Hopkins OMIM database record ID 602648, and in cited publications numbered 858 and 8586 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Collagen, Type XVII, Alpha 1 (COL17A1, Accession NM_000494) is another VGAM1324 host target gene. COL17A1 BINDING SITE1 and COL17A1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL17A1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL17A1 BINDING SITE1 and COL17A1 BINDING SITE2, designated SEQ ID:6107 and SEQ ID:10613 respectively, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46960] Another function of VGAM1324 is therefore inhibition of Collagen, Type XVII, Alpha 1 (COL17A1, Accession NM_000494). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL17A1. Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717) is another VGAM1324 host target gene. DGKI BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by DGKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGKI BINDING SITE, designated SEQ ID:11080, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46961] Another function of VGAM1324 is therefore inhibition of Diacylglycerol Kinase, Iota (DGKI, Accession NM_004717), a gene which regulates the intracellular concentration of the second messenger diacylglycerol (DAG). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGKI. The function of DGKI and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1107. Hermansky-Pudlak Syndrome 1 (HPS1, Accession NM_000195) is another VGAM1324 host target gene. HPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of HPS1 BINDING SITE, designated SEQ ID:5695, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46962] Another function of VGAM1324 is therefore inhibition of Hermansky–Pudlak Syndrome 1 (HPS1, Accession NM_000195). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPS1. Heparan Sulfate 2–O–sulfotransferase 1 (HS2ST1, Accession NM_012262) is another VGAM1324 host target gene. HS2ST1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS2ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS2ST1 BINDING SITE, designated SEQ ID:14579, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46963] Another function of VGAM1324 is therefore inhibition of Heparan Sulfate 2–O–sulfotransferase 1 (HS2ST1, Accession NM_012262). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with HS2ST1. Mitogen-activated Protein Kinase Kinase Kinase 7 Interacting Protein 2 (MAP3K7IP2, Accession NM_015093) is another VGAM1324 host target gene. MAP3K7IP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K7IP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K7IP2 BINDING SITE, designated SEQ ID:17485, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46964] Another function of VGAM1324 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 7 Interacting Protein 2 (MAP3K7IP2, Accession NM_015093). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K7IP2. Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410) is another VGAM1324 host target gene. MGAT5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

MGAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT5 BINDING SITE, designated SEQ ID:8241, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46965] Another function of VGAM1324 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT5. 8-oxoguanine DNA Glycosylase (OGG1, Accession NM_002542) is another VGAM1324 host target gene. OGG1 BINDING SITE1 through OGG1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OGG1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OGG1 BINDING SITE1 through OGG1 BINDING SITE3, designated SEQ ID:8391, SEQ ID:18808 and SEQ ID:18813 respectively, to the nucleotide sequence of

VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46966] Another function of VGAM1324 is therefore inhibition of 8-oxoguanine DNA Glycosylase (OGG1, Accession NM_002542), a gene which is involved in base excision DNA repair and removal of 8-oxyguanine. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OGG1. The function of OGG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM390. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12A (PPP1R12A, Accession NM_002480) is another VGAM1324 host target gene. PPP1R12A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R12A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R12A BINDING SITE, designated SEQ ID:8306, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46967] Another function of VGAM1324 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12A (PPP1R12A, Accession NM_002480), a gene which regulates the interaction of actin and myosin. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R12A. The function of PPP1R12A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM838. Protein Kinase, CGMP-dependent, Type II (PRKG2, Accession NM_006259) is another VGAM1324 host target gene. PRKG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKG2 BINDING SITE, designated SEQ ID:12941, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46968] Another function of VGAM1324 is therefore inhibition of Protein Kinase, CGMP-dependent, Type II (PRKG2, Accession NM_006259), a gene which regulate a great variety of

functions, including smooth muscle relaxation, neuronal excitability, and epithelial electrolyte transport. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKG2. The function of PRKG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM16. TEM6 (Accession NM_022748) is another VGAM1324 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM6 BINDING SITE, designated SEQ ID:22965, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46969] Another function of VGAM1324 is therefore inhibition of TEM6 (Accession NM_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175.BCoR (Accession NM_017745) is another VGAM1324 host target gene. BCoR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCoR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCoR BINDING SITE, designated SEQ ID:19339, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46970] Another function of VGAM1324 is therefore inhibition of BCoR (Accession NM_017745). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCoR. Calmegin (CLGN, Accession NM_004362) is another VGAM1324 host target gene. CLGN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLGN BINDING SITE,

designated SEQ ID:10568, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46971] Another function of VGAM1324 is therefore inhibition of Calmegin (CLGN, Accession NM_004362). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLGN. DKFZP564F013 (Accession XM_168479) is another VGAM1324 host target gene. DKFZP564F013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564F013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564F013 BINDING SITE, designated SEQ ID:45206, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46972] Another function of VGAM1324 is therefore inhibition of DKFZP564F013 (Accession XM_168479). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564F013. DKFZp761F2014 (Accession

NM_020215) is another VGAM1324 host target gene. DKFZp761F2014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761F2014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761F2014 BINDING SITE, designated SEQ ID:21465, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46973] Another function of VGAM1324 is therefore inhibition of DKFZp761F2014 (Accession NM_020215). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761F2014. FLJ10738 (Accession NM_018199) is another VGAM1324 host target gene. FLJ10738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10738 BINDING SITE, designated SEQ ID:20069, to the nucleotide sequence of VGAM1324 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4035.

[46974] Another function of VGAM1324 is therefore inhibition of FLJ10738 (Accession NM_018199). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10738. FLJ13962 (Accession NM_024862) is another VGAM1324 host target gene. FLJ13962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13962 BINDING SITE, designated SEQ ID:24297, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46975] Another function of VGAM1324 is therefore inhibition of FLJ13962 (Accession NM_024862). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13962. FLJ14621 (Accession NM_032811) is another VGAM1324 host target gene. FLJ14621 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14621, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14621 BINDING SITE, designated SEQ ID:26584, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46976] Another function of VGAM1324 is therefore inhibition of FLJ14621 (Accession NM_032811). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14621. FLJ20275 (Accession NM_017737) is another VGAM1324 host target gene. FLJ20275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20275 BINDING SITE, designated SEQ ID:19324, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46977] Another function of VGAM1324 is therefore inhibition of FLJ20275 (Accession NM_017737). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20275. KIAA1013 (Accession XM_114303) is another VGAM1324 host target gene. KIAA1013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1013 BINDING SITE, designated SEQ ID:42858, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46978] Another function of VGAM1324 is therefore inhibition of KIAA1013 (Accession XM_114303). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1013. KIAA1028 (Accession XM_166324) is another VGAM1324 host target gene. KIAA1028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1028 BINDING SITE, designated SEQ ID:44165, to the

nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46979] Another function of VGAM1324 is therefore inhibition of KIAA1028 (Accession XM_166324). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1028. KIAA1254 (Accession XM_046132) is another VGAM1324 host target gene. KIAA1254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1254 BINDING SITE, designated SEQ ID:34700, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46980] Another function of VGAM1324 is therefore inhibition of KIAA1254 (Accession XM_046132). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1254. MGC16175 (Accession NM_032765) is another VGAM1324 host target gene. MGC16175 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by MGC16175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16175 BINDING SITE, designated SEQ ID:26512, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46981] Another function of VGAM1324 is therefore inhibition of MGC16175 (Accession NM_032765). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16175. Neurexophilin 3 (NXPH3, Accession XM_037847) is another VGAM1324 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32722, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46982] Another function of VGAM1324 is therefore inhibition of

Neurexophilin 3 (NXPH3, Accession XM_037847). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. Ring Finger Protein 38 (RNF38, Accession NM_022781) is another VGAM1324 host target gene. RNF38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF38 BINDING SITE, designated SEQ ID:23061, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46983] Another function of VGAM1324 is therefore inhibition of Ring Finger Protein 38 (RNF38, Accession NM_022781). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF38. SP329 (Accession NM_030793) is another VGAM1324 host target gene. SP329 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SP329, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP329 BINDING SITE, designated SEQ ID:25098, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46984] Another function of VGAM1324 is therefore inhibition of SP329 (Accession NM_030793). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP329. LOC145195 (Accession XM_096731) is another VGAM1324 host target gene. LOC145195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145195 BINDING SITE, designated SEQ ID:40517, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46985] Another function of VGAM1324 is therefore inhibition of LOC145195 (Accession XM_096731). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145195. LOC145900 (Accession XM_085276) is another VGAM1324 host target gene. LOC145900 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145900 BINDING SITE, designated SEQ ID:38011, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46986] Another function of VGAM1324 is therefore inhibition of LOC145900 (Accession XM_085276). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145900. LOC149372 (Accession XM_086509) is another VGAM1324 host target gene. LOC149372 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38733, to

the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46987] Another function of VGAM1324 is therefore inhibition of LOC149372 (Accession XM_086509). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC153146 (Accession XM_098319) is another VGAM1324 host target gene. LOC153146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153146 BINDING SITE, designated SEQ ID:41576, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46988] Another function of VGAM1324 is therefore inhibition of LOC153146 (Accession XM_098319). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153146. LOC203378 (Accession XM_117541) is another VGAM1324 host target gene. LOC203378 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC203378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203378 BINDING SITE, designated SEQ ID:43547, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46989] Another function of VGAM1324 is therefore inhibition of LOC203378 (Accession XM_117541). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203378. LOC254778 (Accession XM_171193) is another VGAM1324 host target gene. LOC254778 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254778, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254778 BINDING SITE, designated SEQ ID:45976, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46990] Another function of VGAM1324 is therefore inhibition of LOC254778 (Accession XM_171193). Accordingly, utilities

of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254778. LOC254936 (Accession XM_170770) is another VGAM1324 host target gene. LOC254936 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254936 BINDING SITE, designated SEQ ID:45526, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46991] Another function of VGAM1324 is therefore inhibition of LOC254936 (Accession XM_170770). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254936. LOC51580 (Accession NM_015874) is another VGAM1324 host target gene. LOC51580 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC51580 BINDING SITE, designated SEQ ID:18012, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46992] Another function of VGAM1324 is therefore inhibition of LOC51580 (Accession NM_015874). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51580. LOC90639 (Accession XM_033092) is another VGAM1324 host target gene. LOC90639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90639 BINDING SITE, designated SEQ ID:31833, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46993] Another function of VGAM1324 is therefore inhibition of LOC90639 (Accession XM_033092). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90639. LOC90777 (Accession XM_034052) is another VGAM1324 host target gene. LOC90777 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90777, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90777 BINDING SITE, designated SEQ ID:31990, to the nucleotide sequence of VGAM1324 RNA, herein designated VGAM RNA, also designated SEQ ID:4035.

[46994] Another function of VGAM1324 is therefore inhibition of LOC90777 (Accession XM_034052). Accordingly, utilities of VGAM1324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90777. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1325 (VGAM1325) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[46995] VGAM1325 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1325 was detected is described hereinabove with reference to Figs. 1-8.

[46996] VGAM1325 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Latent Virus.

VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[46997] VGAM1325 gene encodes a VGAM1325 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1325 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1325 precursor RNA is designated SEQ ID:1311, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1311 is located at position 3735 relative to the genome of Garlic Latent Virus.

[46998] VGAM1325 precursor RNA folds onto itself, forming VGAM1325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[46999] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1325 folded precursor RNA into VGAM1325 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1325 RNA is designated SEQ ID:4036, and is provided hereinbelow with reference to the sequence listing part.

[47000] VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1325 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47001] VGAM1325 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1325 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1325 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1325 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47002] The complementary binding of VGAM1325 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1325 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1325 host target RNA into VGAM1325 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47003] It is appreciated that VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1325 host target genes. The mRNA of each one of this plurality of VGAM1325 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1325 RNA, herein designated VGAM RNA, and which when bound by VGAM1325 RNA causes inhibition of translation of respective one or more VGAM1325 host target proteins.

[47004] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1325 gene, herein designated VGAM GENE, on one or more VGAM1325 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47005] It is yet further appreciated that a function of VGAM1325 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1325 include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGAM1325 correlate with, and may be deduced from, the identity of the host target genes which VGAM1325 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47006] Nucleotide sequences of the VGAM1325 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1325 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1325 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1325 are further described hereinbelow with reference to Table 1.

[47007] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1325 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1325 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47008] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1325 gene, herein designated VGAM is inhibition of expression of VGAM1325 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1325 correlate with, and may be deduced from, the identity of the target genes which VGAM1325 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47009] Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512) is a VGAM1325 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12032, to the nucleotide sequence of VGAM1325 RNA, herein designated VGAM RNA, also designated SEQ ID:4036.

[47010] A function of VGAM1325 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512). Accordingly, utilities of VGAM1325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARP. Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055) is another VGAM1325 host target gene. GFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFAP BINDING SITE, designated SEQ ID:7814, to the nucleotide sequence of VGAM1325 RNA, herein designated VGAM RNA, also designated SEQ ID:4036.

[47011] Another function of VGAM1325 is therefore inhibition of Glial Fibrillary Acidic Protein (GFAP, Accession NM_002055). Accordingly, utilities of VGAM1325 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with GFAP. LOC91252 (Accession XM_037173) is another VGAM1325 host target gene. LOC91252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91252 BINDING SITE, designated SEQ ID:32551, to the nucleotide sequence of VGAM1325 RNA, herein designated VGAM RNA, also designated SEQ ID:4036.

[47012] Another function of VGAM1325 is therefore inhibition of LOC91252 (Accession XM_037173). Accordingly, utilities of VGAM1325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91252. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1326 (VGAM1326) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47013] VGAM1326 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1326 was detected is described hereinabove with reference to Figs. 1–8.

[47014] VGAM1326 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus.

VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47015] VGAM1326 gene encodes a VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1326 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1326 precursor RNA is designated SEQ ID:1312, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1312 is located at position 91066 relative to the genome of Myxoma Virus.

[47016] VGAM1326 precursor RNA folds onto itself, forming VGAM1326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47017] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1326 folded precursor RNA into VGAM1326 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1326 RNA is designated SEQ ID:4037, and is provided hereinbelow with reference to the sequence listing part.

[47018] VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1326 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47019] VGAM1326 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1326 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1326 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47020] The complementary binding of VGAM1326 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1326 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1326 host target RNA into VGAM1326 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47021] It is appreciated that VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1326 host target genes. The mRNA of each one of this plurality of VGAM1326 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1326 RNA, herein designated VGAM RNA, and which when bound by VGAM1326 RNA causes inhibition of translation of respective one or more VGAM1326 host target proteins.

[47022] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1326 gene, herein designated VGAM GENE, on one or more VGAM1326 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47023] It is yet further appreciated that a function of VGAM1326 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1326 correlate with, and may be deduced from, the identity of the host target genes which VGAM1326 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47024] Nucleotide sequences of the VGAM1326 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1326 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1326 are further described hereinbelow with reference to Table 1.

[47025] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1326 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1326 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47026] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1326 gene, herein designated VGAM is inhibition of expression of VGAM1326 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1326 correlate with, and may be deduced from, the identity of the target genes which VGAM1326 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47027] Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692) is a VGAM1326 host target gene. ALDH1B1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by ALDH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH1B1 BINDING SITE, designated SEQ ID:6347, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47028] A function of VGAM1326 is therefore inhibition of Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH1B1. Complement Component 7 (C7, Accession NM_000587) is another VGAM1326 host target gene. C7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7 BINDING SITE, designated SEQ ID:6187, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47029] Another function of VGAM1326 is therefore inhibition of Complement Component 7 (C7, Accession NM_000587). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7. Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM_035453) is another VGAM1326 host target gene. CLASP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLASP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLASP2 BINDING SITE, designated SEQ ID:32266, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47030] Another function of VGAM1326 is therefore inhibition of Cytoplasmic Linker Associated Protein 2 (CLASP2, Accession XM_035453), a gene which is involved in the regional regulation of microtubule dynamics in motile fibroblasts. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLASP2. The function of CLASP2 and its association with various diseases and clinical condi-

tions, has been established by previous studies, as described hereinabove with reference to VGAM897. Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391) is another VGAM1326 host target gene. CYP8B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP8B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP8B1 BINDING SITE, designated SEQ ID:10620, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47031] Another function of VGAM1326 is therefore inhibition of Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391), a gene which functions in bile acid biosynthesis. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP8B1. The function of CYP8B1 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM923.Decorin (DCN, Accession NM_133507) is another VGAM1326 host target gene. DCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCN BINDING SITE, designated SEQ ID:28574, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47032] Another function of VGAM1326 is therefore inhibition of Decorin (DCN, Accession NM_133507), a gene which may mediate in epithelial/mesenchymal interactions . Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCN. The function of DCN has been established by previous studies. Decorin and biglycan (OMIM Ref. No. 301870) are related but distinct small proteoglycans found in many connective tissues. Danielson et al. (1993) found that the human decorin gene spans more than 38 kb and contains 8 exons and very large introns, 2 of which are 5.4 and more than 13.2 kb. They discovered 2

alternatively spliced leader exons, Ia and Ib, in the 5-prime untranslated region. Using Northern blotting or reverse transcriptase PCR, they detected the 2 leader exons in a variety of mRNAs isolated from human cell lines and tissues. Sequences highly homologous (OMIM Ref. No. 74–87%) to exons Ia and Ib were found in the 5-prime untranslated region of avian and bovine decorin, respectively. This high degree of conservation among species suggested regulatory functions for these leader exons. In situ hybridization studies of developing mouse embryos suggested that decorin may play a role in epithelial/mesenchymal interactions during organ development and shaping (Scholzen et al., 1994). Dyne et al. (1996) studied 2 patients with osteogenesis imperfecta and the same gly415-to-ser mutation of the COL1A1 gene (120150.0044), but a different clinical expression. They speculated that these differences could be the result of abnormalities in other connective tissue proteins. Since decorin is a component of connective tissue, binds to type I collagen fibrils, and plays a role in matrix assembly, they studied decorin production in skin fibroblasts from these 2 patients. Cultured fibroblasts from the patient with extremely severe osteogenesis imperfecta (classified as type

II/III) were found to secrete barely detectable amounts of decorin into culture medium. Northern blot analysis showed decorin mRNA levels below the limit of detection. The patient with a less severe phenotype had fibroblasts that expressed decorin normally. Dyne et al. (1996) suggested that the different clinical phenotypes could be due to the differing genetic backgrounds of the patients, such that in the more severely affected patient the absence of decorin aggravated the clinical phenotype.

[47033] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47034] Scholzen, T.; Solursh, M.; Suzuki, S.; Reiter, R.; Morgan, J. L.; Buchberg, A. M.; Siracusa, L. D.; Iozzo, R. V. : The murine decorin: complete cDNA cloning, genomic organization, chromosomal assignment, and expression during organogenesis and tissue differentiation. *J. Biol. Chem.* 269: 28270–28281, 1994. ; and

[47035] Dyne, K. M.; Valli, M.; Forlino, A.; Mottes, M.; Kresse, H.; Cetta, G. : Deficient expression of the small proteoglycan decorin in a case of severe/lethal osteogenesis imperfecta. *Am. J.*

[47036] Further studies establishing the function and utilities of

DCN are found in John Hopkins OMIM database record ID 125255, and in cited publications numbered 1989–1998 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DEK Oncogene (DNA binding) (DEK, Accession NM_003472) is another VGAM1326 host target gene. DEK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DEK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEK BINDING SITE, designated SEQ ID:9536, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47037] Another function of VGAM1326 is therefore inhibition of DEK Oncogene (DNA binding) (DEK, Accession NM_003472), a gene which interacts in transcriptional regulation and signal transduction. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEK. The function of DEK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM795.EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838) is another VGAM1326 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41887, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47038] Another function of VGAM1326 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. MAP-kinase Activating Death Domain (MADD, Accession NM_130470) is another VGAM1326 host target gene. MADD BINDING SITE1 through MADD BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MADD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of MADD BINDING SITE1 through MADD BINDING SITE6, designated SEQ ID:28234, SEQ ID:28250, SEQ ID:28245, SEQ ID:28240, SEQ ID:28255 and SEQ ID:9785 respectively, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47039] Another function of VGAM1326 is therefore inhibition of MAP-kinase Activating Death Domain (MADD, Accession NM_130470), a gene which may regulate two different pathways for neural activities.interacts with the type-1 tumor necrosis factor receptor (TNFR1); death domain-containing protein. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADD. The function of MADD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.NKX3A (Accession NM_006167) is another VGAM1326 host target gene. NKX3A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NKX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of NKX3A BINDING SITE, designated SEQ ID:12831, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47040] Another function of VGAM1326 is therefore inhibition of NKX3A (Accession NM_006167), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKX3A. The function of NKX3A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM481. Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM1326 host target gene. SEDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEDL BINDING SITE, designated SEQ ID:15903, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47041] Another function of VGAM1326 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Splicing Factor, Arginine/serine-rich 2, Interacting Protein (SFRS2IP, Accession NM_004719) is another VGAM1326 host target gene. SFRS2IP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SFRS2IP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS2IP BINDING SITE, designated SEQ ID:11085, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47042] Another function of VGAM1326 is therefore inhibition of Splicing Factor, Arginine/serine-rich 2, Interacting Protein

(SFRS2IP, Accession NM_004719), a gene which plays an essential role in pre-mRNA splicing. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS2IP. The function of SFRS2IP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM700. Translin (TSN, Accession NM_004622) is another VGAM1326 host target gene. TSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSN BINDING SITE, designated SEQ ID:10988, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47043] Another function of VGAM1326 is therefore inhibition of Translin (TSN, Accession NM_004622), a gene which is a DNA binding protein and involved in DNA repair, replication, or recombination. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSN. The function

of TSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98. Visinin-like 1 (VSNL1, Accession NM_003385) is another VGAM1326 host target gene. VSNL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VSNL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VSNL1 BINDING SITE, designated SEQ ID:9419, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47044] Another function of VGAM1326 is therefore inhibition of Visinin-like 1 (VSNL1, Accession NM_003385). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VSNL1. Vitronectin (serum spreading factor, somatomedin B, complement S-protein) (VTN, Accession NM_000638) is another VGAM1326 host target gene. VTN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VTN, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VTN BINDING SITE, designated SEQ ID:6274, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47045] Another function of VGAM1326 is therefore inhibition of Vitronectin (serum spreading factor, somatomedin B, complement S-protein) (VTN, Accession NM_000638), a gene which is a cell adhesion and spreading factor found in serum and tissues. Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VTN. The function of VTN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM850.Ac-like Transposable Element (ALTE, Accession NM_004729) is another VGAM1326 host target gene. ALTE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALTE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALTE BINDING SITE, designated SEQ ID:11108, to the nu-

cleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47046] Another function of VGAM1326 is therefore inhibition of Ac-like Transposable Element (ALTE, Accession NM_004729). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALTE. Ankyrin Repeat and SOCS Box-containing 16 (ASB16, Accession NM_080863) is another VGAM1326 host target gene. ASB16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASB16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASB16 BINDING SITE, designated SEQ ID:28107, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47047] Another function of VGAM1326 is therefore inhibition of Ankyrin Repeat and SOCS Box-containing 16 (ASB16, Accession NM_080863). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASB16. Chromosome 11 Open Reading Frame 17 (C11orf17, Accession

NM_020642) is another VGAM1326 host target gene. C11orf17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf17 BINDING SITE, designated SEQ ID:21805, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47048] Another function of VGAM1326 is therefore inhibition of Chromosome 11 Open Reading Frame 17 (C11orf17, Accession NM_020642). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf17. Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945) is another VGAM1326 host target gene. C21orf25 BINDING SITE1 and C21orf25 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C21orf25, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf25 BIND-

ING SITE1 and C21orf25 BINDING SITE2, designated SEQ ID:31797 and SEQ ID:31803 respectively, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47049] Another function of VGAM1326 is therefore inhibition of Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf25. Carbohydrate (chondroitin) Synthase 1 (CHSY1, Accession NM_014918) is another VGAM1326 host target gene. CHSY1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHSY1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHSY1 BINDING SITE, designated SEQ ID:17171, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47050] Another function of VGAM1326 is therefore inhibition of Carbohydrate (chondroitin) Synthase 1 (CHSY1, Accession NM_014918). Accordingly, utilities of VGAM1326 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CHSY1. DKFZP434B044 (Accession NM_031476) is another VGAM1326 host target gene. DKFZP434B044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434B044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B044 BINDING SITE, designated SEQ ID:25552, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47051] Another function of VGAM1326 is therefore inhibition of DKFZP434B044 (Accession NM_031476). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B044. DKFZp761F2014 (Accession NM_020215) is another VGAM1326 host target gene. DKFZp761F2014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761F2014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZp761F2014 BINDING SITE, designated SEQ ID:21462, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47052] Another function of VGAM1326 is therefore inhibition of DKFZp761F2014 (Accession NM_020215). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761F2014. DKFZp761N1114 (Accession XM_086327) is another VGAM1326 host target gene. DKFZp761N1114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761N1114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N1114 BINDING SITE, designated SEQ ID:38604, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47053] Another function of VGAM1326 is therefore inhibition of DKFZp761N1114 (Accession XM_086327). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp761N1114. FLJ10640 (Accession NM_019023) is another VGAM1326 host target gene. FLJ10640 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10640, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10640 BINDING SITE, designated SEQ ID:21111, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47054] Another function of VGAM1326 is therefore inhibition of FLJ10640 (Accession NM_019023). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10640. FLJ13114 (Accession NM_024541) is another VGAM1326 host target gene. FLJ13114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13114 BINDING SITE, designated SEQ ID:23748, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM

RNA, also designated SEQ ID:4037.

[47055] Another function of VGAM1326 is therefore inhibition of FLJ13114 (Accession NM_024541). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13114. FLJ13197 (Accession NM_024614) is another VGAM1326 host target gene. FLJ13197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13197 BINDING SITE, designated SEQ ID:23871, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47056] Another function of VGAM1326 is therefore inhibition of FLJ13197 (Accession NM_024614). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13197. FLJ13456 (Accession XM_038291) is another VGAM1326 host target gene. FLJ13456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13456, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13456 BINDING SITE, designated SEQ ID:32796, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47057] Another function of VGAM1326 is therefore inhibition of FLJ13456 (Accession XM_038291). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13456. FLJ14442 (Accession NM_032785) is another VGAM1326 host target gene. FLJ14442 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14442 BINDING SITE, designated SEQ ID:26533, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47058] Another function of VGAM1326 is therefore inhibition of FLJ14442 (Accession NM_032785). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14442. FLJ20004 (Accession XM_170889) is another VGAM1326 host target gene. FLJ20004 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20004 BINDING SITE, designated SEQ ID:45645, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47059] Another function of VGAM1326 is therefore inhibition of FLJ20004 (Accession XM_170889). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20004. FLJ22531 (Accession NM_024650) is another VGAM1326 host target gene. FLJ22531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22531 BINDING SITE, designated SEQ ID:23943, to the nucleotide

sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47060] Another function of VGAM1326 is therefore inhibition of FLJ22531 (Accession NM_024650). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22531. FLJ23263 (Accession NM_025115) is another VGAM1326 host target gene. FLJ23263 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23263 BINDING SITE, designated SEQ ID:24765, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47061] Another function of VGAM1326 is therefore inhibition of FLJ23263 (Accession NM_025115). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23263. FLJ31101 (Accession NM_017964) is another VGAM1326 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ31101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19682, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47062] Another function of VGAM1326 is therefore inhibition of FLJ31101 (Accession NM_017964). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31101. GBTS1 (Accession NM_145173) is another VGAM1326 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29732, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47063] Another function of VGAM1326 is therefore inhibition of GBTS1 (Accession NM_145173). Accordingly, utilities of

VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1. GL004 (Accession XM_038373) is another VGAM1326 host target gene. GL004 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GL004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GL004 BINDING SITE, designated SEQ ID:32830, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47064] Another function of VGAM1326 is therefore inhibition of GL004 (Accession XM_038373). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GL004. KIAA0417 (Accession XM_048898) is another VGAM1326 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0417 BINDING SITE,

designated SEQ ID:35294, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47065] Another function of VGAM1326 is therefore inhibition of KIAA0417 (Accession XM_048898). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA0475 (Accession NM_014864) is another VGAM1326 host target gene. KIAA0475 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0475 BINDING SITE, designated SEQ ID:16946, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47066] Another function of VGAM1326 is therefore inhibition of KIAA0475 (Accession NM_014864). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0475. KIAA0561 (Accession XM_038150) is another VGAM1326 host target gene. KIAA0561 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0561, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0561 BINDING SITE, designated SEQ ID:32763, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47067] Another function of VGAM1326 is therefore inhibition of KIAA0561 (Accession XM_038150). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0561. KIAA0594 (Accession XM_036117) is another VGAM1326 host target gene. KIAA0594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0594 BINDING SITE, designated SEQ ID:32385, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47068] Another function of VGAM1326 is therefore inhibition of

KIAA0594 (Accession XM_036117). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0594. KIAA0720 (Accession XM_030970) is another VGAM1326 host target gene. KIAA0720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0720 BINDING SITE, designated SEQ ID:31230, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47069] Another function of VGAM1326 is therefore inhibition of KIAA0720 (Accession XM_030970). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0720. KIAA1054 (Accession XM_043493) is another VGAM1326 host target gene. KIAA1054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1054 BINDING SITE, designated SEQ ID:33952, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47070] Another function of VGAM1326 is therefore inhibition of KIAA1054 (Accession XM_043493). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1054. KIAA1143 (Accession XM_044014) is another VGAM1326 host target gene. KIAA1143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1143 BINDING SITE, designated SEQ ID:34071, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47071] Another function of VGAM1326 is therefore inhibition of KIAA1143 (Accession XM_044014). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1143. KIAA1373 (Accession XM_048195) is another

VGAM1326 host target gene. KIAA1373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1373 BINDING SITE, designated SEQ ID:35122, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47072] Another function of VGAM1326 is therefore inhibition of KIAA1373 (Accession XM_048195). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1373. KIAA1649 (Accession NM_032311) is another VGAM1326 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1649 BINDING SITE, designated SEQ ID:26102, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47073] Another function of VGAM1326 is therefore inhibition of KIAA1649 (Accession NM_032311). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. KIAA1655 (Accession XM_039442) is another VGAM1326 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33081, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47074] Another function of VGAM1326 is therefore inhibition of KIAA1655 (Accession XM_039442). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1655. KIAA1971 (Accession XM_058720) is another VGAM1326 host target gene. KIAA1971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1971, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1971 BINDING SITE, designated SEQ ID:36727, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47075] Another function of VGAM1326 is therefore inhibition of KIAA1971 (Accession XM_058720). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1971. MGC2477 (Accession NM_024099) is another VGAM1326 host target gene. MGC2477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2477 BINDING SITE, designated SEQ ID:23540, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47076] Another function of VGAM1326 is therefore inhibition of MGC2477 (Accession NM_024099). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC2477. MGC5149 (Accession XM_051200) is another VGAM1326 host target gene. MGC5149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5149 BINDING SITE, designated SEQ ID:35782, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47077] Another function of VGAM1326 is therefore inhibition of MGC5149 (Accession XM_051200). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5149. Paternally Expressed 10 (PEG10, Accession NM_015068) is another VGAM1326 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17423, to the nucleotide sequence of VGAM1326 RNA,

herein designated VGAM RNA, also designated SEQ ID:4037.

[47078] Another function of VGAM1326 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM_015068). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651) is another VGAM1326 host target gene. PELI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PELI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI1 BINDING SITE, designated SEQ ID:21814, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47079] Another function of VGAM1326 is therefore inhibition of Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI1. SCAMP-4 (Accession NM_079834) is another VGAM1326 host target gene.

SCAMP-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP-4 BINDING SITE, designated SEQ ID:27818, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47080] Another function of VGAM1326 is therefore inhibition of SCAMP-4 (Accession NM_079834). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP-4. Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM_022978) is another VGAM1326 host target gene. SERF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERF1B BINDING SITE, designated SEQ ID:23256, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4037.

[47081] Another function of VGAM1326 is therefore inhibition of Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM_022978). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERF1B. SS-56 (Accession XM_006063) is another VGAM1326 host target gene. SS-56 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SS-56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS-56 BINDING SITE, designated SEQ ID:29988, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47082] Another function of VGAM1326 is therefore inhibition of SS-56 (Accession XM_006063). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS-56. Serine/threonine Kinase 33 (STK33, Accession XM_031831) is another VGAM1326 host target gene. STK33 BINDING SITE is HOST TARGET binding site found

in the 5` untranslated region of mRNA encoded by STK33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK33 BINDING SITE, designated SEQ ID:31495, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47083] Another function of VGAM1326 is therefore inhibition of Serine/threonine Kinase 33 (STK33, Accession XM_031831). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK33. SUN1 (Accession NM_025154) is another VGAM1326 host target gene. SUN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SUN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUN1 BINDING SITE, designated SEQ ID:24792, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47084] Another function of VGAM1326 is therefore inhibition of

SUN1 (Accession NM_025154). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUN1. LOC112724 (Accession NM_138412) is another VGAM1326 host target gene. LOC112724 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC112724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112724 BINDING SITE, designated SEQ ID:28778, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47085] Another function of VGAM1326 is therefore inhibition of LOC112724 (Accession NM_138412). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112724. LOC112817 (Accession NM_138413) is another VGAM1326 host target gene. LOC112817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC112817 BINDING SITE, designated SEQ ID:28780, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47086] Another function of VGAM1326 is therefore inhibition of LOC112817 (Accession NM_138413). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112817. LOC135398 (Accession XM_069333) is another VGAM1326 host target gene. LOC135398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135398 BINDING SITE, designated SEQ ID:37385, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47087] Another function of VGAM1326 is therefore inhibition of LOC135398 (Accession XM_069333). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135398. LOC146050 (Accession XM_085301) is an-

other VGAM1326 host target gene. LOC146050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146050 BINDING SITE, designated SEQ ID:38053, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47088] Another function of VGAM1326 is therefore inhibition of LOC146050 (Accession XM_085301). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146050. LOC152220 (Accession XM_098176) is another VGAM1326 host target gene. LOC152220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152220 BINDING SITE, designated SEQ ID:41440, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47089] Another function of VGAM1326 is therefore inhibition of LOC152220 (Accession XM_098176). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152220. LOC152300 (Accession XM_087432) is another VGAM1326 host target gene. LOC152300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152300 BINDING SITE, designated SEQ ID:39249, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47090] Another function of VGAM1326 is therefore inhibition of LOC152300 (Accession XM_087432). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152300. LOC158293 (Accession XM_088541) is another VGAM1326 host target gene. LOC158293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158293, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158293 BINDING SITE, designated SEQ ID:39807, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47091] Another function of VGAM1326 is therefore inhibition of LOC158293 (Accession XM_088541). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158293. LOC196264 (Accession XM_113683) is another VGAM1326 host target gene. LOC196264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196264 BINDING SITE, designated SEQ ID:42331, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47092] Another function of VGAM1326 is therefore inhibition of LOC196264 (Accession XM_113683). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196264. LOC200316 (Accession XM_114205) is another VGAM1326 host target gene. LOC200316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200316 BINDING SITE, designated SEQ ID:42795, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47093] Another function of VGAM1326 is therefore inhibition of LOC200316 (Accession XM_114205). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200316. LOC200471 (Accession XM_117234) is another VGAM1326 host target gene. LOC200471 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200471 BINDING SITE, designated SEQ ID:43304, to the nucleotide sequence of VGAM1326 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4037.

[47094] Another function of VGAM1326 is therefore inhibition of LOC200471 (Accession XM_117234). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200471. LOC202908 (Accession XM_114602) is another VGAM1326 host target gene. LOC202908 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202908 BINDING SITE, designated SEQ ID:42994, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47095] Another function of VGAM1326 is therefore inhibition of LOC202908 (Accession XM_114602). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202908. LOC203350 (Accession XM_117536) is another VGAM1326 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43529, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47096] Another function of VGAM1326 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC220074 (Accession NM_145309) is another VGAM1326 host target gene. LOC220074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220074 BINDING SITE, designated SEQ ID:29822, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47097] Another function of VGAM1326 is therefore inhibition of LOC220074 (Accession NM_145309). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC220074. LOC221477 (Accession XM_166397) is another VGAM1326 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44259, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47098] Another function of VGAM1326 is therefore inhibition of LOC221477 (Accession XM_166397). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC254249 (Accession XM_170931) is another VGAM1326 host target gene. LOC254249 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC254249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254249 BINDING SITE, designated SEQ ID:45712, to

the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47099] Another function of VGAM1326 is therefore inhibition of LOC254249 (Accession XM_170931). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254249. LOC50999 (Accession NM_016040) is another VGAM1326 host target gene. LOC50999 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC50999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC50999 BINDING SITE, designated SEQ ID:18119, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47100] Another function of VGAM1326 is therefore inhibition of LOC50999 (Accession NM_016040). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC50999. LOC90141 (Accession XM_029373) is another VGAM1326 host target gene. LOC90141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC90141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90141 BINDING SITE, designated SEQ ID:30879, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47101] Another function of VGAM1326 is therefore inhibition of LOC90141 (Accession XM_029373). Accordingly, utilities of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90141. LOC93276 (Accession XM_050200) is another VGAM1326 host target gene. LOC93276 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC93276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93276 BINDING SITE, designated SEQ ID:35589, to the nucleotide sequence of VGAM1326 RNA, herein designated VGAM RNA, also designated SEQ ID:4037.

[47102] Another function of VGAM1326 is therefore inhibition of LOC93276 (Accession XM_050200). Accordingly, utilities

of VGAM1326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93276. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1327 (VGAM1327) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47103] VGAM1327 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1327 was detected is described hereinabove with reference to Figs. 1-8.

[47104] VGAM1327 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47105] VGAM1327 gene encodes a VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1327 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1327 precursor RNA is designated SEQ ID:1313, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1313 is located at position 86115 relative to the genome of Myxoma Virus.

- [47106] VGAM1327 precursor RNA folds onto itself, forming VGAM1327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47107] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1327 folded precursor RNA into VGAM1327 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1327 RNA is designated SEQ ID:4038, and

is provided hereinbelow with reference to the sequence listing part.

[47108] VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1327 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[47109] VGAM1327 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1327 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1327 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47110] The complementary binding of VGAM1327 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1327 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1327 host target RNA into VGAM1327 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47111] It is appreciated that VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1327 host target genes. The mRNA of each one of this plurality of VGAM1327 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1327 RNA, herein designated VGAM RNA, and which when bound by VGAM1327 RNA causes inhibition of translation of respective one or more VGAM1327 host target proteins.

[47112] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1327 gene, herein designated VGAM GENE, on one or more VGAM1327 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47113] It is yet further appreciated that a function of VGAM1327 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1327 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1327 correlate with, and may be deduced from, the identity of the host target genes which VGAM1327 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47114] Nucleotide sequences of the VGAM1327 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1327 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1327 are further described hereinbelow with reference to Table 1.

[47115] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1327 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1327 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47116] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1327 gene, herein designated VGAM is inhibition of expression of VGAM1327 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1327 correlate with, and may be deduced from, the identity of the target genes which VGAM1327 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47117] Coronin, Actin Binding Protein, 2B (CORO2B, Accession XM_035403) is a VGAM1327 host target gene. CORO2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CORO2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO2B BINDING SITE, designated SEQ ID:32256, to the nucleotide sequence of VGAM1327 RNA, herein designated VGAM RNA, also designated SEQ ID:4038.

[47118] A function of VGAM1327 is therefore inhibition of Coronin, Actin Binding Protein, 2B (CORO2B, Accession XM_035403), a gene which may play a role in the reorganization of neuronal actin structure. Accordingly, utilities of VGAM1327 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with CORO2B. The function of CORO2B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269) is another VGAM1327 host target gene. LEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEF1 BINDING SITE, designated SEQ ID:18391, to the nucleotide sequence of VGAM1327 RNA, herein designated VGAM RNA, also designated SEQ ID:4038.

[47119] Another function of VGAM1327 is therefore inhibition of Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269), a gene which plays an essential role in the formation of several organs and structures that require inductive tissue interactions. Accordingly, utilities of VGAM1327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEF1. The function of LEF1 and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1328 (VGAM1328) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47120] VGAM1328 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1328 was detected is described hereinabove with reference to Figs. 1-8.

[47121] VGAM1328 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47122] VGAM1328 gene encodes a VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1328 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1328 precursor RNA is designated SEQ ID:1314, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1314 is located at position 84471 relative to the genome of Myxoma Virus.

- [47123] VGAM1328 precursor RNA folds onto itself, forming VGAM1328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47124] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1328 folded precursor RNA into VGAM1328 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1328 RNA is designated SEQ ID:4039, and

is provided hereinbelow with reference to the sequence listing part.

[47125] VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1328 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[47126] VGAM1328 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1328 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1328 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47127] The complementary binding of VGAM1328 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1328 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1328 host target RNA into VGAM1328 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47128] It is appreciated that VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1328 host target genes. The mRNA of each one of this plurality of VGAM1328 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1328 RNA, herein designated VGAM RNA, and which when bound by VGAM1328 RNA causes inhibition of translation of respective one or more VGAM1328 host target proteins.

[47129] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1328 gene, herein designated VGAM GENE, on one or more VGAM1328 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47130] It is yet further appreciated that a function of VGAM1328 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM1328 correlate with, and may be deduced from, the identity of the host target genes which VGAM1328 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47131] Nucleotide sequences of the VGAM1328 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1328 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1328 are further described hereinbelow with reference to Table 1.

[47132] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1328 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1328 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47133] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1328 gene, herein designated VGAM is inhibition of expression of VGAM1328 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1328 correlate with, and may be deduced from, the identity of the target genes which VGAM1328 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47134] Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223) is a VGAM1328 host target gene. ITPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR2 BINDING SITE, designated SEQ ID:7994, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47135] A function of VGAM1328 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR2. Solute Carrier Family 19 (thiamine transporter), Member 2 (SLC19A2, Accession

XM_044421) is another VGAM1328 host target gene. SLC19A2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC19A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A2 BINDING SITE, designated SEQ ID:34195, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47136] Another function of VGAM1328 is therefore inhibition of Solute Carrier Family 19 (thiamine transporter), Member 2 (SLC19A2, Accession XM_044421). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A2. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966) is another VGAM1328 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE,

designated SEQ ID:27534, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47137] Another function of VGAM1328 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. Chromosome 20 Open Reading Frame 82 (C20orf82, Accession XM_097736) is another VGAM1328 host target gene. C20orf82 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf82, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf82 BINDING SITE, designated SEQ ID:41084, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47138] Another function of VGAM1328 is therefore inhibition of Chromosome 20 Open Reading Frame 82 (C20orf82, Accession XM_097736). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with C20orf82.

KIAA0217 (Accession XM_040265) is another VGAM1328 host target gene. KIAA0217 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0217 BINDING SITE, designated SEQ ID:33277, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47139] Another function of VGAM1328 is therefore inhibition of KIAA0217 (Accession XM_040265). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0217. KIAA0729 (Accession XM_171027) is another VGAM1328 host target gene. KIAA0729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0729 BINDING SITE, designated SEQ ID:45806, to the

nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47140] Another function of VGAM1328 is therefore inhibition of KIAA0729 (Accession XM_171027). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0729. LOC253017 (Accession XM_171068) is another VGAM1328 host target gene. LOC253017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253017 BINDING SITE, designated SEQ ID:45870, to the nucleotide sequence of VGAM1328 RNA, herein designated VGAM RNA, also designated SEQ ID:4039.

[47141] Another function of VGAM1328 is therefore inhibition of LOC253017 (Accession XM_171068). Accordingly, utilities of VGAM1328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253017. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1329 (VGAM1329) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47142] VGAM1329 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1329 was detected is described hereinabove with reference to Figs. 1–8.

[47143] VGAM1329 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Virus C. VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47144] VGAM1329 gene encodes a VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1329 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1329 precursor RNA is designated SEQ ID:1315, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1315 is located at position 7174 relative to the genome of Garlic Virus C.

[47145] VGAM1329 precursor RNA folds onto itself, forming VGAM1329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47146] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1329 folded precursor RNA into VGAM1329 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1329 RNA is designated SEQ ID:4040, and is provided hereinbelow with reference to the sequence listing part.

[47147] VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1329 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1329 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47148] VGAM1329 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1329 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1329 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47149] The complementary binding of VGAM1329 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1329 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1329 host target RNA into VGAM1329 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47150] It is appreciated that VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1329 host target genes. The mRNA of each one of this plurality of VGAM1329 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1329 RNA, herein designated VGAM RNA, and which when bound by VGAM1329 RNA causes inhibition of translation of respective one or more VGAM1329 host target proteins.

[47151] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1329 gene, herein designated VGAM GENE, on one or more VGAM1329 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47152] It is yet further appreciated that a function of VGAM1329 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of viral infection by Garlic Virus C. Specific functions, and accordingly utilities, of VGAM1329 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1329 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47153] Nucleotide sequences of the VGAM1329 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1329 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1329 are further described hereinbelow with reference to Table 1.

[47154] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1329 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1329 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47155] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1329 gene, herein designated VGAM is inhibition of expression of VGAM1329 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1329 correlate with, and may be deduced from, the identity of the target genes which VGAM1329

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47156] Chromosome 20 Open Reading Frame 4 (C20orf4, Accession NM_015511) is a VGAM1329 host target gene.

C20orf4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf4 BINDING SITE, designated SEQ ID:17770, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47157] A function of VGAM1329 is therefore inhibition of Chromosome 20 Open Reading Frame 4 (C20orf4, Accession NM_015511). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf4. Chromosome 9 Open Reading Frame 7 (C9orf7, Accession NM_017586) is another VGAM1329 host target gene. C9orf7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C9orf7, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf7 BINDING SITE, designated SEQ ID:19034, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47158] Another function of VGAM1329 is therefore inhibition of Chromosome 9 Open Reading Frame 7 (C9orf7, Accession NM_017586). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf7. DKFZP762D096 (Accession XM_037662) is another VGAM1329 host target gene. DKFZP762D096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP762D096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP762D096 BINDING SITE, designated SEQ ID:32663, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47159] Another function of VGAM1329 is therefore inhibition of DKFZP762D096 (Accession XM_037662). Accordingly, utilities of VGAM1329 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP762D096. FLJ10829 (Accession NM_018234) is another VGAM1329 host target gene. FLJ10829 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10829 BINDING SITE, designated SEQ ID:20176, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47160] Another function of VGAM1329 is therefore inhibition of FLJ10829 (Accession NM_018234). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10829. KIAA0255 (Accession NM_014742) is another VGAM1329 host target gene. KIAA0255 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0255 BINDING SITE, designated SEQ ID:16412, to the

nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47161] Another function of VGAM1329 is therefore inhibition of KIAA0255 (Accession NM_014742). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0255. LOC143909 (Accession XM_096506) is another VGAM1329 host target gene. LOC143909 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143909 BINDING SITE, designated SEQ ID:40386, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47162] Another function of VGAM1329 is therefore inhibition of LOC143909 (Accession XM_096506). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143909. LOC151996 (Accession XM_098151) is another VGAM1329 host target gene. LOC151996 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC151996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151996 BINDING SITE, designated SEQ ID:41411, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47163] Another function of VGAM1329 is therefore inhibition of LOC151996 (Accession XM_098151). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151996. LOC254042 (Accession XM_171022) is another VGAM1329 host target gene. LOC254042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254042 BINDING SITE, designated SEQ ID:45790, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47164] Another function of VGAM1329 is therefore inhibition of LOC254042 (Accession XM_171022). Accordingly, utilities

of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254042. LOC256158 (Accession XM_175125) is another VGAM1329 host target gene. LOC256158 BINDING SITE1 and LOC256158 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC256158, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE1 and LOC256158 BINDING SITE2, designated SEQ ID:46614 and SEQ ID:46615 respectively, to the nucleotide sequence of VGAM1329 RNA, herein designated VGAM RNA, also designated SEQ ID:4040.

[47165] Another function of VGAM1329 is therefore inhibition of LOC256158 (Accession XM_175125). Accordingly, utilities of VGAM1329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1330 (VGAM1330) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[47166] VGAM1330 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1330 was detected is described hereinabove with reference to Figs. 1–8.

[47167] VGAM1330 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A. VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47168] VGAM1330 gene encodes a VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1330 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1330 precursor RNA is designated SEQ ID:1316, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1316 is located at position 27688 relative to the genome of Human Adenovirus A.

[47169] VGAM1330 precursor RNA folds onto itself, forming VGAM1330 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47170] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1330 folded precursor RNA into VGAM1330 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1330 RNA is designated SEQ ID:4041, and is provided hereinbelow with reference to the sequence listing part.

[47171] VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1330 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47172] VGAM1330 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1330 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1330 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47173] The complementary binding of VGAM1330 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1330 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1330 host target RNA into VGAM1330 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47174] It is appreciated that VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1330 host target genes. The mRNA of each one of this plurality of VGAM1330 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1330 RNA, herein designated VGAM RNA, and which when bound by VGAM1330 RNA causes inhibition of translation of respective one or more VGAM1330 host target proteins.

[47175] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1330 gene, herein designated VGAM GENE, on one or more VGAM1330 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47176] It is yet further appreciated that a function of VGAM1330 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGAM1330 correlate with, and may be deduced from, the identity of the host target genes which VGAM1330 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[47177] Nucleotide sequences of the VGAM1330 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1330 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1330 are further described hereinbelow with reference to Table 1.

[47178] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1330 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1330 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47179] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1330 gene, herein designated VGAM is inhibition of expression of VGAM1330 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1330 correlate with, and may be deduced from, the identity of the target genes which VGAM1330 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47180] SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 3 (SMARCA3, Accession NM_003071) is a VGAM1330 host target gene. SMARCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMARCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCA3 BINDING SITE, designated SEQ ID:9039, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47181] A function of VGAM1330 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 3 (SMARCA3, Accession NM_003071), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCA3. The function of SMARCA3 has been established by previous studies. Chromatin remodeling enzymes are implicated in a variety of important cellular functions. Various components of chromatin remodeling complexes,

including several members of the SWI/SNF family, are disrupted in cancer. Moinova et al. (2002) identified the HLTF gene (SMARCA3) as a target for gene inactivation in colon cancer. Loss of HLTF expression accompanied by HLTF promoter methylation was noted in 9 of 34 colon cancer cell lines. In these cell lines, HLTF expression was restored by treatment with the demethylating agent 5-azacytidine. In further studies of primary colon cancer tissues, HLTF methylation was detected in 27 of 63 cases (43%). No methylation of HLTF was detected in breast or lung cancers, suggesting selection for HLTF methylation in colonic malignancies. Transfection of HLTF suppressed 75% of colon growth in each of 3 different HLTF-deficient cell lines, but showed no suppressive effect in any of 3 HLTF-proficient cell lines. These findings showed that HLTF is a common target for methylation and epigenetic gene silencing in colon cancer and suggested HLTF as a candidate colon cancer suppressor gene.

[47182] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47183] Moinova, H. R.; Chen, W.-D.; Shen, L.; Smiraglia, D.; Olechnowicz, J.; Ravi, L.; Kasturi, L.; Myeroff, L.; Plass, C.;

Parsons, R.; Minna, J.; Willson, J. K. V.; Green, S. B.; Issa, J.-P.; Markowitz, S. D. : HLTF gene silencing in human colon cancer. Proc. Nat. Acad. Sci. 99: 4562–4567, 2002. ; and

[47184] Sheridan, P. L.; Schorpp, Ding, H.; Descheemaeker, K.; Marynen, P.; Nelles, L.; Carvalho, T.; Carmo-Fonseca, M.; Collen, D.; Belayew, A. : Characterization of a helicase-like transcrip.

[47185] Further studies establishing the function and utilities of SMARCA3 are found in John Hopkins OMIM database record ID 603257, and in cited publications numbered 8496–8499 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Thromboxane A2 Receptor (TBXA2R, Accession NM_001060) is another VGAM1330 host target gene. TBXA2R BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TBXA2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBXA2R BINDING SITE, designated SEQ ID:6726, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ

ID:4041.

[47186] Another function of VGAM1330 is therefore inhibition of Thromboxane A2 Receptor (TBXA2R, Accession NM_001060), a gene which activates Ca^{2+} -activated chloride channels; stimulates platelet aggregation and smooth muscle constriction. Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBXA2R. The function of TBXA2R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.FLJ22843 (Accession NM_025184) is another VGAM1330 host target gene. FLJ22843 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22843 BINDING SITE, designated SEQ ID:24820, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47187] Another function of VGAM1330 is therefore inhibition of FLJ22843 (Accession NM_025184). Accordingly, utilities of

VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22843. KIAA1465 (Accession XM_027396) is another VGAM1330 host target gene. KIAA1465 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1465 BINDING SITE, designated SEQ ID:30499, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47188] Another function of VGAM1330 is therefore inhibition of KIAA1465 (Accession XM_027396). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1465. KIAA1958 (Accession XM_088566) is another VGAM1330 host target gene. KIAA1958 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1958 BINDING SITE, designated SEQ ID:39833, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47189] Another function of VGAM1330 is therefore inhibition of KIAA1958 (Accession XM_088566). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1958. PRO1770 (Accession NM_014100) is another VGAM1330 host target gene. PRO1770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1770, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1770 BINDING SITE, designated SEQ ID:15327, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47190] Another function of VGAM1330 is therefore inhibition of PRO1770 (Accession NM_014100). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1770. PTD012 (Accession NM_014039) is another VGAM1330 host target gene. PTD012 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTD012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTD012 BINDING SITE, designated SEQ ID:15268, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47191] Another function of VGAM1330 is therefore inhibition of PTD012 (Accession NM_014039). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTD012. Sorting Nexin 10 (SNX10, Accession NM_013322) is another VGAM1330 host target gene. SNX10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNX10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX10 BINDING SITE, designated SEQ ID:14969, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47192] Another function of VGAM1330 is therefore inhibition of

Sorting Nexin 10 (SNX10, Accession NM_013322). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX10. Striatin, Calmodulin Binding Protein 3 (STRN3, Accession NM_014574) is another VGAM1330 host target gene. STRN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRN3 BINDING SITE, designated SEQ ID:15934, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47193] Another function of VGAM1330 is therefore inhibition of Striatin, Calmodulin Binding Protein 3 (STRN3, Accession NM_014574). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRN3. LOC221931 (Accession XM_168348) is another VGAM1330 host target gene. LOC221931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221931, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221931 BINDING SITE, designated SEQ ID:45120, to the nucleotide sequence of VGAM1330 RNA, herein designated VGAM RNA, also designated SEQ ID:4041.

[47194] Another function of VGAM1330 is therefore inhibition of LOC221931 (Accession XM_168348). Accordingly, utilities of VGAM1330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221931. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1331 (VGAM1331) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47195] VGAM1331 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1331 was detected is described hereinabove with reference to Figs. 1-8.

[47196] VGAM1331 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A.

VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47197] VGAM1331 gene encodes a VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1331 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1331 precursor RNA is designated SEQ ID:1317, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1317 is located at position 25669 relative to the genome of Human Adenovirus A.

[47198] VGAM1331 precursor RNA folds onto itself, forming VGAM1331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47199] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1331 folded precursor RNA into VGAM1331 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1331 RNA is designated SEQ ID:4042, and is provided hereinbelow with reference to the sequence listing part.

[47200] VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1331 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47201] VGAM1331 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1331 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1331 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47202] The complementary binding of VGAM1331 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1331 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1331 host target RNA into VGAM1331 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47203] It is appreciated that VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1331 host target genes. The mRNA of each one of this plurality of VGAM1331 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1331 RNA, herein designated VGAM RNA, and which when bound by VGAM1331 RNA causes inhibition of translation of respective one or more VGAM1331 host target proteins.

[47204] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1331 gene, herein designated VGAM GENE, on one or more VGAM1331 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47205] It is yet further appreciated that a function of VGAM1331 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1331 include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGAM1331 correlate with, and may be deduced from, the identity of the host target genes which VGAM1331 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47206] Nucleotide sequences of the VGAM1331 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1331 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1331 are further described hereinbelow with reference to Table 1.

[47207] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1331 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1331 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47208] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1331 gene, herein designated VGAM is inhibition of expression of VGAM1331 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1331 correlate with, and may be deduced from, the identity of the target genes which VGAM1331 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47209] Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM_114191) is a VGAM1331 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ

ID:42770, to the nucleotide sequence of VGAM1331 RNA, herein designated VGAM RNA, also designated SEQ ID:4042.

[47210] A function of VGAM1331 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM_114191). Accordingly, utilities of VGAM1331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. LOC168391 (Accession XM_095061) is another VGAM1331 host target gene. LOC168391 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168391 BINDING SITE, designated SEQ ID:40243, to the nucleotide sequence of VGAM1331 RNA, herein designated VGAM RNA, also designated SEQ ID:4042.

[47211] Another function of VGAM1331 is therefore inhibition of LOC168391 (Accession XM_095061). Accordingly, utilities of VGAM1331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168391. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1332 (VGAM1332) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47212] VGAM1332 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1332 was detected is described hereinabove with reference to Figs. 1–8.

[47213] VGAM1332 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A. VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47214] VGAM1332 gene encodes a VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1332 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1332 precursor RNA is designated SEQ ID:1318, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1318 is located at position 26522 relative to the genome of Human Adenovirus A.

[47215] VGAM1332 precursor RNA folds onto itself, forming VGAM1332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47216] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1332 folded precursor RNA into VGAM1332 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1332 RNA is designated SEQ ID:4043, and is provided hereinbelow with reference to the sequence listing part.

[47217] VGAM1332 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1332 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47218] VGAM1332 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1332 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1332 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1332 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[47219] The complementary binding of VGAM1332 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1332 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1332 host target RNA into VGAM1332 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47220] It is appreciated that VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1332 host target genes. The mRNA of each one of this plurality of VGAM1332 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1332 RNA, herein designated VGAM RNA, and which when bound by VGAM1332 RNA causes inhibition of translation of respective one or more

VGAM1332 host target proteins.

[47221] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1332 gene, herein designated VGAM GENE, on one or more VGAM1332 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47222] It is yet further appreciated that a function of VGAM1332 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Spe-

cific functions, and accordingly utilities, of VGAM1332 correlate with, and may be deduced from, the identity of the host target genes which VGAM1332 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47223] Nucleotide sequences of the VGAM1332 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1332 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1332 are further described hereinbelow with reference to Table 1.

[47224] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1332 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1332 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47225] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1332 gene, herein designated VGAM is inhibition of expression of VGAM1332 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1332 correlate with, and may be deduced from, the identity of the target genes which VGAM1332 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47226] Chloride Channel 3 (CLCN3, Accession NM_001829) is a VGAM1332 host target gene. CLCN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN3 BINDING SITE, designated SEQ ID:7563, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47227] A function of VGAM1332 is therefore inhibition of Chloride Channel 3 (CLCN3, Accession NM_001829), a gene which play a role in the neural cell function through regulation of membrane excitability. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN3. The function of CLCN3 has been established by previous studies. Cid et al. (1995) cloned a human homolog of the rat voltage-gated chloride channel CLC2 from a T84 ep-

ithelial cell cDNA library. The predicted 898–amino acid protein is over 93% identical to the rat sequence. The gene was mapped to 3q26–qter by PCR of somatic cell hybrid DNAs. Schwiebert et al. (1998) found that CLC2 chloride channels are expressed in epithelia affected by cystic fibrosis (CF; 219700) and raised the possibility that these might represent an alternative target for pharmacotherapy of CF. To explore this possibility, they manipulated genetically the expression levels of CLC2 channels in airway epithelial cells derived from cystic fibrosis patients.

Whole–cell patch–clamp analysis of cells overexpressing CLC2 identified hyperpolarization–activated chloride ion currents (HACCs) that displayed time– and voltage–dependent activation and an inwardly rectifying steady–state current voltage relationship. Reduction of extracellular pH to 5.0 caused significant increases in HACCs in overexpressing cells and the appearance of robust currents in parental cells from the cystic fibrosis patient. CF cells stably transfected with the antisense CLC2 cDNA showed reduced expression of CLC2 compared with parental cells by Western blotting, and a significant reduction in the magnitude of pH–dependent HACCs. To determine whether changes in the extracellular pH alone could initiate chlo–

ride transport via CLC2 channels, they performed chloride-36 efflux studies on overexpressing cells and cells with endogenous expression of CLC2. Acidic extracellular pH increased chloride-36 efflux rates in both cell types, although the CLC2-overexpressing cells had significantly greater chloride conduction and a longer duration of efflux than the parental cells. Compounds that exploit the pH mechanism of activating endogenous CLC2 channels may provide a pharmacologic option for increasing chloride conductance in airways of CF patients.

[47228] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47229] Cid, L. P.; Montrose-Rafizadeh, C.; Smith, D. I.; Guggino, W. B.; Cutting, G. R. : Cloning of a putative human voltage-gated chloride channel (CLC-2) cDNA widely expressed in human tissues. *Hum. Molec. Genet.* 4: 407-413, 1995. ; and

[47230] Schwiebert, E. M.; Cid-Soto, L. P.; Stafford, D.; Carter, M.; Blaisdell, C. J.; Zeitlin, P. L.; Guggino, W. B.; Cutting, G. R. : Analysis of CLC-2 channels as an alternative pathway for.

[47231] Further studies establishing the function and utilities of CLCN3 are found in John Hopkins OMIM database record

ID 600580, and in cited publications numbered 10180–10183, 377 and 10184 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interferon Regulatory Factor 2 (IRF2, Accession NM_002199) is another VGAM1332 host target gene. IRF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRF2 BINDING SITE, designated SEQ ID:7956, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47232] Another function of VGAM1332 is therefore inhibition of Interferon Regulatory Factor 2 (IRF2, Accession NM_002199), a gene which is a transcriptional activator of type I interferon and interferon-inducible genes. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRF2. The function of IRF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM511. LIM Domain Containing Pre-

ferred Translocation Partner In Lipoma (LPP, Accession NM_005578) is another VGAM1332 host target gene. LPP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPP BINDING SITE, designated SEQ ID:12106, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47233] Another function of VGAM1332 is therefore inhibition of LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM_005578). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPP. Membrane Metallo-endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10) (MME, Accession NM_007288) is another VGAM1332 host target gene. MME BINDING SITE1 through MME BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MME, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MME BINDING SITE1 through MME BINDING SITE4, designated SEQ ID:14152, SEQ ID:6600, SEQ ID:14148 and SEQ ID:14156 respectively, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47234] Another function of VGAM1332 is therefore inhibition of Membrane Metallo–endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10) (MME, Accession NM_007288), a gene which is thermolysin–like specificity. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MME. The function of MME has been established by previous studies. Common acute lymphocytic leukemia antigen is an important cell surface marker in the diagnosis of human acute lymphocytic leukemia (ALL). It is present on leukemic cells of pre–B phenotype, which represent 85% of cases of ALL. CALLA is not restricted to leukemic cells, however, and is found on a variety of normal tissues. CALLA is a glycoprotein that is particularly abundant in kidney, where it is present on the brush border of proximal tubules and on glomerular epithelium. Letarte et al. (1988) cloned a cDNA coding for

CALLA and showed that the amino acid sequence deduced from the cDNA sequence is identical to that of human membrane-associated neutral endopeptidase (NEP; EC 3.4.24.11), also known as enkephalinase. NEP cleaves peptides at the amino side of hydrophobic residues and inactivates several peptide hormones including glucagon, enkephalins, substance P, neurotensin, oxytocin, and bradykinin. By cDNA transfection analysis, Shipp et al. (1989) confirmed that CALLA is a functional neutral endopeptidase of the type that has previously been called enkephalinase. Barker et al. (1989) demonstrated that the CALLA gene, which encodes a 100-kD type II transmembrane glycoprotein, exists in a single copy of greater than 45 kb which is not rearranged in malignancies expressing cell surface CALLA. D'Adamio et al. (1989) demonstrated that the CALLA gene spans more than 80 kb and is composed of 24 exons. Animal model experiments lend further support to the function of MME. Amyloid-beta peptide (OMIM Ref. No. 104760), the pathogenic agent of Alzheimer disease (OMIM Ref. No. 104300), is a physiologic metabolite in the brain. Iwata et al. (2001) examined the role of neprilysin, a candidate amyloid-beta degrading peptidase, in the metabolism using neprilysin gene-

disrupted mice. Neprilysin deficiency resulted in defects both in the degradation of exogenously administered amyloid-beta and in the metabolic suppression of the endogenous amyloid-beta levels in a gene dose-dependent manner. The regional levels of amyloid-beta in the neprilysin-deficient mouse brain were in the distinct order of hippocampus, cortex, thalamus/striatum, and cerebellum, where hippocampus has the highest level and cerebellum the lowest, correlating with the vulnerability to amyloid-beta deposition in brains of humans with Alzheimer disease. Iwata et al. (2001) concluded that even partial downregulation of neprilysin activity, which could be caused by aging, can contribute to Alzheimer disease by promoting amyloid-beta accumulation.

[47235] It is appreciated that the abovementioned animal model for MME is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[47236] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47237] Iwata, N.; Tsubuki, S.; Takaki, Y.; Shirotani, K.; Lu, B.; Gerard, N. P.; Gerard, C.; Hama, E.; Lee, H.-J.; Saido, T. C. :

Metabolic regulation of brain A-beta by neprilysin. Science 292: 1550-1552, 2001. ; and

[47238] Letarte, M.; Vera, S.; Tran, R.; Addis, J. B. L.; Onizuka, R. J.; Quackenbush, E. J.; Jongeneel, C. V.; McInnes, R. R. : Common acute lymphocytic leukemia antigen is identical to neutr.

[47239] Further studies establishing the function and utilities of MME are found in John Hopkins OMIM database record ID 120520, and in cited publications numbered 12226-12228, 413 and 12229-12231 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinoblastoma Binding Protein 8 (RBBP8, Accession NM_002894) is another VGAM1332 host target gene. RBBP8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RBBP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBBP8 BINDING SITE, designated SEQ ID:8801, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47240] Another function of VGAM1332 is therefore inhibition of

Retinoblastoma Binding Protein 8 (RBBP8, Accession NM_002894), a gene which may be a tumor suppressor. Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBBP8. The function of RBBP8 has been established by previous studies. Fusco et al. (1998) described the isolation and characterization of a cDNA encoding a polypeptide, named RIM for 'retinoblastoma-interacting myosin-like,' that interacted in a yeast 2-hybrid system as well as in mammalian cells with the retinoblastoma (RB; 180200) protein. The RIM cDNA predicts a 897-amino acid polypeptide containing 2 leucine zipper motifs, an RB-binding domain, and a CTBP (see OMIM Ref. No. 602618)-binding domain. The RIM protein has weak homology to myosin family (see OMIM Ref. No. 160720) proteins throughout its length. Northern blot analysis revealed a ubiquitously expressed 3.6-kb mRNA. Immunoprecipitation experiments revealed that a truncated RIM protein containing amino acids 142-897 interacts with RB in mammalian cells. To understand the mechanism by which interaction between E1A and CTBP results in tumorigenesis-restraining activity, Schaeper et al. (1998) searched for cellular proteins that complex with CTBP. By

a yeast 2-hybrid screen and RACE PCR, Schaeper et al. (1998) identified and cloned a CTBP-interacting protein (CTIP). CTIP contains a 5-amino acid motif, the PLDLS motif, that is highly conserved among E1A proteins of all human adenoviruses. CTIP binds to CTBP via the PLDLS motif. Yu et al. (1998) used the Sos recruitment system to screen for proteins that bind to the region of BRCA1 (OMIM Ref. No. 113705) containing the BRCT domains. Yu et al. (1998) found that the BRCT domains interact in vivo with CTIP, a protein identified on the basis of its association with the CTBP transcriptional corepressor (Schaeper et al., 1998). Yu et al. (1998) concluded that BRCA1 regulates gene expression, at least in part, by modulating CTBP-mediated transcriptional repression. Moreover, Yu et al. (1998) found that the in vivo interaction between BRCA1 and CTIP is completely ablated by each of 3 independent tumor-associated mutations affecting the BRCT motifs of BRCA1. Yu et al. (1998) concluded that BRCA1-CTIP interaction may be required for tumor suppression by BRCA1.

[47241] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [47242] Fusco, C.; Reymond, A.; Zervos, A. S. : Molecular cloning and characterization of a novel retinoblastoma-binding protein. *Genomics* 51: 351–358, 1998. ; and
- [47243] Yu, X.; Wu, L. C.; Bowcock, A. M.; Aronheim, A.; Baer, R. : The C-terminal (BRCT) domains of BRCA1 interact in vivo with CtIP, a protein implicated in the CtBP pathway of transcriptional.
- [47244] Further studies establishing the function and utilities of RBBP8 are found in John Hopkins OMIM database record ID 604124, and in cited publications numbered 740 and 7406–7409 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BM–002 (Accession NM_016617) is another VGAM1332 host target gene. BM–002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BM–002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM–002 BINDING SITE, designated SEQ ID:18723, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.
- [47245] Another function of VGAM1332 is therefore inhibition of

BM-002 (Accession NM_016617). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM-002. KIAA0855 (Accession NM_015003) is another VGAM1332 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17375, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47246] Another function of VGAM1332 is therefore inhibition of KIAA0855 (Accession NM_015003). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0855. KIAA0871 (Accession NM_014961) is another VGAM1332 host target gene. KIAA0871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0871 BINDING SITE, designated SEQ ID:17331, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47247] Another function of VGAM1332 is therefore inhibition of KIAA0871 (Accession NM_014961). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0871. KIAA1843 (Accession XM_030838) is another VGAM1332 host target gene. KIAA1843 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1843 BINDING SITE, designated SEQ ID:31162, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47248] Another function of VGAM1332 is therefore inhibition of KIAA1843 (Accession XM_030838). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1843. Kelch-like 4 (Drosophila) (KLHL4, Accession

NM_019117) is another VGAM1332 host target gene. KLHL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL4 BINDING SITE, designated SEQ ID:21191, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47249] Another function of VGAM1332 is therefore inhibition of Kelch-like 4 (Drosophila) (KLHL4, Accession NM_019117). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL4. OCT11 (Accession NM_014352) is another VGAM1332 host target gene. OCT11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OCT11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCT11 BINDING SITE, designated SEQ ID:15679, to the nucleotide sequence of VGAM1332 RNA,

herein designated VGAM RNA, also designated SEQ ID:4043.

[47250] Another function of VGAM1332 is therefore inhibition of OCT11 (Accession NM_014352). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCT11. Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842) is another VGAM1332 host target gene. SPRY2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SPRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPRY2 BINDING SITE, designated SEQ ID:12454, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47251] Another function of VGAM1332 is therefore inhibition of Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPRY2. Spermatid Perinuclear RNA Binding Protein (STRBP, Accession NM_018387)

is another VGAM1332 host target gene. STRBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STRBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRBP BINDING SITE, designated SEQ ID:20420, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47252] Another function of VGAM1332 is therefore inhibition of Spermatid Perinuclear RNA Binding Protein (STRBP, Accession NM_018387). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRBP. TIP47 (Accession NM_005817) is another VGAM1332 host target gene. TIP47 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIP47, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIP47 BINDING SITE, designated SEQ ID:12416, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47253] Another function of VGAM1332 is therefore inhibition of TIP47 (Accession NM_005817). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIP47. LOC200268 (Accession XM_114178) is another VGAM1332 host target gene. LOC200268 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200268 BINDING SITE, designated SEQ ID:42763, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47254] Another function of VGAM1332 is therefore inhibition of LOC91818 (Accession XM_040878). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91818. LOC91818 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91818, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91818 BINDING SITE, designated SEQ ID:33404, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47255] Another function of VGAM1332 is therefore inhibition of LOC91818 (Accession XM_040878). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91818. LOC92573 (Accession XM_045884) is another VGAM1332 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34598, to the nucleotide sequence of VGAM1332 RNA, herein designated VGAM RNA, also designated SEQ ID:4043.

[47256] Another function of VGAM1332 is therefore inhibition of LOC92573 (Accession XM_045884). Accordingly, utilities of VGAM1332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92573. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1333 (VGAM1333) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47257] VGAM1333 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1333 was detected is described hereinabove with reference to Figs. 1–8.

[47258] VGAM1333 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A. VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47259] VGAM1333 gene encodes a VGAM1333 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1333 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1333 precursor RNA is designated SEQ ID:1319, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1319 is located at position 24338 relative to the genome of Human Adenovirus A.

- [47260] VGAM1333 precursor RNA folds onto itself, forming VGAM1333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47261] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1333 folded precursor RNA into VGAM1333 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1333 RNA is designated SEQ ID:4044, and is provided hereinbelow with reference to the sequence listing part.

[47262] VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1333 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47263] VGAM1333 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1333 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1333 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47264] The complementary binding of VGAM1333 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1333 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1333 host target RNA into VGAM1333 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47265] It is appreciated that VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1333 host target genes. The mRNA of each one of this plurality of VGAM1333 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1333 RNA, herein designated VGAM RNA, and which when bound by VGAM1333 RNA causes

inhibition of translation of respective one or more VGAM1333 host target proteins.

[47266] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1333 gene, herein designated VGAM GENE, on one or more VGAM1333 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47267] It is yet further appreciated that a function of VGAM1333 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1333 include diagnosis, prevention and

treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGAM1333 correlate with, and may be deduced from, the identity of the host target genes which VGAM1333 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47268] Nucleotide sequences of the VGAM1333 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1333 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1333 are further described hereinbelow with reference to Table 1.

[47269] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1333 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1333 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47270] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1333 gene, herein designated VGAM is inhibition of expression of VGAM1333 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1333 correlate with, and may be deduced from, the identity of the target genes which VGAM1333 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47271] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778) is a VGAM1333 host target gene. B4GALT4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT4 BINDING SITE, designated SEQ ID:9859, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47272] A function of VGAM1333 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT4. Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409) is another VGAM1333 host

target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10664, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47273] Another function of VGAM1333 is therefore inhibition of Dystrophin Myotonic-protein Kinase (DMPK, Accession NM_004409). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. Neuroepithelial Cell Transforming Gene 1 (NET1, Accession NM_005863) is another VGAM1333 host target gene. NET1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NET1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NET1 BINDING SITE, designated SEQ ID:12476, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA,

also designated SEQ ID:4044.

[47274] Another function of VGAM1333 is therefore inhibition of Neuroepithelial Cell Transforming Gene 1 (NET1, Accession NM_005863), a gene which is induced morphologic alterations and conferred a malignant phenotype in vitro and in nude mice. Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NET1. The function of NET1 has been established by previous studies. Pacholczyk et al. (1991) isolated a cDNA encoding a human noradrenaline transporter. The cDNA sequence predicted a protein of 617 amino acids, with 12–13 highly hydrophobic regions compatible with membrane-spanning domains. Expression of the cDNA clone in transfected HeLa cells indicated that noradrenaline transport activity is sodium-dependent and sensitive to selective noradrenaline transport inhibitors. Transporter RNA was localized to the brain stem and adrenal. The predicted protein sequence demonstrated significant amino acid identity with the Na(+)/gamma-aminobutyric acid transporter, thus identifying a new gene family for neurotransmitter transporter proteins. Pacholczyk et al. (1991) suggested that analysis of the structure and function of this trans-

porter may aid structure-based drug design for the treatment of human depression and lead to a determination of whether transporter abnormalities underlie affective disorders. By hybridization of a panel of somatic cell hybrids and by fluorescence in situ hybridization to metaphase chromosomes, Bruss et al. (1993) mapped the NET1 gene to 16q12.2. Gelernter et al. (1993) reported a TaqI RFLP at the NET1 locus. Gelernter et al. (1993) used PCR with a somatic cell hybrid panel to obtain a provisional assignment of the NET1 gene to chromosome 16. They typed the genetic polymorphism at the NET1 locus in 3 large multigenerational families and, by linkage analysis, confirmed the preliminary assignment and refined the localization to 16q, near the haptoglobin locus (HP; 140100). They then typed the NET1 RFLP on the CEPH families; the additional linkage data localized NET1 to 16q13-q21, flanked by D16S71 centromerically and HP telomerically.

[47275] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47276] Gelernter, J.; Kruger, S.; Pakstis, A. J.; Pacholczyk, T.; Sparkes, R. S.; Kidd, K. K.; Amara, S. : Assignment of the norepinephrine transporter protein (NET1) locus to chro-

mosome 16. Genomics 18: 690–692, 1993. ; and

[47277] Pacholczyk, T.; Blakely, R. D.; Amara, S. G. : Expression cloning of a cocaine– and antidepressant–sensitive human noradrenaline transporter. Nature 350: 350–354, 1991.

[47278] Further studies establishing the function and utilities of NET1 are found in John Hopkins OMIM database record ID 163970, and in cited publications numbered 10785–10796 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Retinoschisis (X–linked, juvenile) 1 (RS1, Accession NM_000330) is another VGAM1333 host target gene. RS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RS1 BINDING SITE, designated SEQ ID:5875, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47279] Another function of VGAM1333 is therefore inhibition of Retinoschisis (X–linked, juvenile) 1 (RS1, Accession NM_000330). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clini–

cal conditions associated with RS1. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728) is another VGAM1333 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38835, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47280] Another function of VGAM1333 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. DKFZP586C1619 (Accession XM_030350) is another VGAM1333 host target gene. DKFZP586C1619 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP586C1619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of DKFZP586C1619 BINDING SITE, designated SEQ ID:31018, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47281] Another function of VGAM1333 is therefore inhibition of DKFZP586C1619 (Accession XM_030350). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586C1619. FLJ13593 (Accession NM_024780) is another VGAM1333 host target gene. FLJ13593 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13593, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13593 BINDING SITE, designated SEQ ID:24149, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47282] Another function of VGAM1333 is therefore inhibition of FLJ13593 (Accession NM_024780). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13593. My015 (Accession XM_039512) is another

VGAM1333 host target gene. My015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by My015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of My015 BINDING SITE, designated SEQ ID:33106, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47283] Another function of VGAM1333 is therefore inhibition of My015 (Accession XM_039512). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with My015. PIP3-E (Accession XM_039749) is another VGAM1333 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33176, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47284] Another function of VGAM1333 is therefore inhibition of PIP3-E (Accession XM_039749). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. LOC129011 (Accession XM_059326) is another VGAM1333 host target gene. LOC129011 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC129011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129011 BINDING SITE, designated SEQ ID:36964, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47285] Another function of VGAM1333 is therefore inhibition of LOC129011 (Accession XM_059326). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129011. LOC204301 (Accession XM_115306) is another VGAM1333 host target gene. LOC204301 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC204301, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204301 BINDING SITE, designated SEQ ID:43092, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47286] Another function of VGAM1333 is therefore inhibition of LOC204301 (Accession XM_115306). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204301. LOC253805 (Accession XM_172854) is another VGAM1333 host target gene. LOC253805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253805 BINDING SITE, designated SEQ ID:46133, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47287] Another function of VGAM1333 is therefore inhibition of LOC253805 (Accession XM_172854). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC253805. LOC254358 (Accession XM_170771) is another VGAM1333 host target gene. LOC254358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254358 BINDING SITE, designated SEQ ID:45530, to the nucleotide sequence of VGAM1333 RNA, herein designated VGAM RNA, also designated SEQ ID:4044.

[47288] Another function of VGAM1333 is therefore inhibition of LOC254358 (Accession XM_170771). Accordingly, utilities of VGAM1333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254358. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1334 (VGAM1334) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47289] VGAM1334 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1334 was detected is described hereinabove with reference to Figs. 1–8.

[47290] VGAM1334 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A. VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47291] VGAM1334 gene encodes a VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1334 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1334 precursor RNA is designated SEQ ID:1320, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1320 is located at position 28536 relative to the genome of Human Adenovirus A.

[47292] VGAM1334 precursor RNA folds onto itself, forming VGAM1334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47293] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1334 folded precursor RNA into VGAM1334 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1334 RNA is designated SEQ ID:4045, and is provided hereinbelow with reference to the sequence listing part.

[47294] VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1334 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47295] VGAM1334 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1334 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1334 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47296] The complementary binding of VGAM1334 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1334 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1334 host target RNA into VGAM1334 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47297] It is appreciated that VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1334 host target genes. The mRNA of each one of this plurality of VGAM1334 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1334 RNA, herein designated VGAM RNA, and which when bound by VGAM1334 RNA causes inhibition of translation of respective one or more VGAM1334 host target proteins.

[47298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1334 gene, herein designated VGAM GENE, on one or more VGAM1334 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47299] It is yet further appreciated that a function of VGAM1334 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGAM1334 correlate with, and may be deduced from, the identity of the host target genes which VGAM1334 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47300] Nucleotide sequences of the VGAM1334 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1334 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1334 are further described hereinbelow with reference to Table 1.

[47301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1334 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1334 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47302] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1334 gene, herein designated VGAM is inhibition of expression of VGAM1334 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1334 correlate with, and may be deduced from, the identity of the target genes which VGAM1334 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47303] Coagulation Factor III (thromboplastin, tissue factor) (F3, Accession XM_040465) is a VGAM1334 host target gene. F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F3, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F3 BINDING SITE, designated SEQ ID:33295, to the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, also designated SEQ ID:4045.

[47304] A function of VGAM1334 is therefore inhibition of Coagulation Factor III (thromboplastin, tissue factor) (F3, Accession XM_040465), a gene which functions in normal hemostasis. Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F3. The function of F3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM817. Ubiquitin Specific Protease 14 (tRNA-guanine transglycosylase) (USP14, Accession NM_005151) is another VGAM1334 host target gene. USP14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP14 BINDING SITE, des-

ignated SEQ ID:11626, to the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, also designated SEQ ID:4045.

[47305] Another function of VGAM1334 is therefore inhibition of Ubiquitin Specific Protease 14 (tRNA-guanine transglycosylase) (USP14, Accession NM_005151), a gene which is similar to ubiquitin-specific cysteine (thiol) proteases and tRNA-guanine transglycosylase. Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP14. The function of USP14 has been established by previous studies. Using Tgt purified from rabbit erythrocytes, Deshpande et al. (1996) measured significant tRNA-guanine transglycosylase activity. Noting significant sequence similarity between Tgt and the deubiquitinating enzyme family, they proposed that Tgt may act as a signal to link deficiency of the transglycosylase product, queuosine, to the ubiquitin-dependent proteolytic pathway for the removal of abnormal or inappropriately expressed proteins. The International Radiation Hybrid Mapping Consortium mapped the USP14 gene to chromosome 18 (SJGC-11272). Wilson et al. (2002) stated that 2 human neurologic disorders possibly involving alterations of

synaptic function map to 18p near USP14: major affective disorder-1 (MAFD1; 125480) and schizophrenia disorder 8 (SCZD8; 603206). Animal model experiments lend further support to the function of USP14. Mice that are homozygous with respect to the spontaneous mutation ax(J) in the ataxia (ax) gene develop severe tremors by 2 to 3 weeks of age followed by hindlimb paralysis and death by 6 to 10 weeks of age. Wilson et al. (2002) showed that ax encodes Usp14, one of the large family of cysteine proteases that specifically feed ubiquitin conjugates. Although Usp14 can cleave a ubiquitin-tagged protein in vitro, it is unable to process polyubiquitin, which is believed to be associated with the protein aggregates seen in Parkinson disease, spinocerebellar ataxia type 1 (SCA1; 164400), and gracile axonal dystrophy (GAD) in mice. The physiologic substrate of Usp14 may therefore contain a monoubiquitin side chain, the removal of which would regulate processes such as protein localization and protein activity. Expression of Usp14 is altered in homozygous ax(J) mice as a result of the insertion of an intracisternal A particle (IAP) into intron 5 of Usp14. In contrast to other neurodegenerative disorders such as Parkinson disease and SCA1 in humans and GAD in mice, neither ubiq-

ubiquitin-positive protein aggregates nor neuronal cell loss was detectable in the CNS of ax(J) mice. Instead, these mice had defects in synaptic transmission in both the central and peripheral nervous systems. These results suggested that ubiquitin proteases are important in regulating synaptic activity in mammals.

[47306] It is appreciated that the abovementioned animal model for USP14 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[47307] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47308] Deshpande, K. L.; Seubert, P. H.; Tillman, D. M.; Farkas, W. R.; Katze, J. R. : Cloning and characterization of cDNA encoding the rabbit tRNA-guanine transglycosylase 60-kilodalton subunit. Arch. Biochem. Biophys. 326: 1-7, 1996. ; and

[47309] Wilson, S. M.; Bhattacharyya, B.; Rachel, R. A.; Coppola, V.; Tessarollo, L.; Householder, D. B.; Fletcher, C. F.; Miller, R. J.; Copeland, N. G.; Jenkins, N. A. : Synaptic defects in at.

[47310] Further studies establishing the function and utilities of USP14 are found in John Hopkins OMIM database record

ID 607274, and in cited publications numbered 5389–5390 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177) is another VGAM1334 host target gene. C17orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf26 BINDING SITE, designated SEQ ID:29184, to the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, also designated SEQ ID:4045.

[47311] Another function of VGAM1334 is therefore inhibition of Chromosome 17 Open Reading Frame 26 (C17orf26, Accession NM_139177). Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf26. MO25 (Accession NM_016289) is another VGAM1334 host target gene. MO25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MO25, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MO25 BINDING SITE, designated SEQ ID:18413, to the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, also designated SEQ ID:4045.

[47312] Another function of VGAM1334 is therefore inhibition of MO25 (Accession NM_016289). Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MO25. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617) is another VGAM1334 host target gene. SLC11A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A2 BINDING SITE, designated SEQ ID:6227, to the nucleotide sequence of VGAM1334 RNA, herein designated VGAM RNA, also designated SEQ ID:4045.

[47313] Another function of VGAM1334 is therefore inhibition of

Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617). Accordingly, utilities of VGAM1334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1335 (VGAM1335) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47314] VGAM1335 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1335 was detected is described hereinabove with reference to Figs. 1-8.

[47315] VGAM1335 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus A. VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47316] VGAM1335 gene encodes a VGAM1335 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1335 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1335 precursor RNA is designated SEQ ID:1321, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1321 is located at position 27935 relative to the genome of Human Adenovirus A.

[47317] VGAM1335 precursor RNA folds onto itself, forming VGAM1335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47318] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1335 folded precursor RNA into VGAM1335 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1335 RNA is designated SEQ ID:4046, and is provided hereinbelow with reference to the sequence listing part.

[47319] VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1335 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[47320] VGAM1335 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1335 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1335 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47321] The complementary binding of VGAM1335 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1335 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1335 host target RNA into VGAM1335 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47322] It is appreciated that VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1335 host target genes. The mRNA of each one of this plurality of VGAM1335 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1335 RNA, herein designated VGAM RNA, and which when bound by VGAM1335 RNA causes inhibition of translation of respective one or more VGAM1335 host target proteins.

[47323] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1335 gene, herein designated VGAM GENE, on one or more VGAM1335 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47324] It is yet further appreciated that a function of VGAM1335 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGAM1335 correlate with, and may be deduced from, the identity of the host target genes which VGAM1335 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47325] Nucleotide sequences of the VGAM1335 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1335 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1335 are further described hereinbelow with reference to Table 1.

[47326] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1335 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1335 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[47327] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1335 gene, herein designated VGAM is inhibition of expression of VGAM1335 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1335 correlate with, and may be deduced from, the identity of the target genes which VGAM1335 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47328] Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 6 (CHST6, Accession NM_021615) is a VGAM1335 host target gene. CHST6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST6 BINDING SITE, designated SEQ ID:22244, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47329] A function of VGAM1335 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 6 (CHST6, Accession NM_021615). Accordingly, utilities of

VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST6. Retinoblastoma 1 (including osteosarcoma) (RB1, Accession XM_165641) is another VGAM1335 host target gene. RB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RB1 BINDING SITE, designated SEQ ID:43705, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47330] Another function of VGAM1335 is therefore inhibition of Retinoblastoma 1 (including osteosarcoma) (RB1, Accession XM_165641), a gene which probably acts as a regulator of other genes. Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RB1. The function of RB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Zinc Finger Protein 2 (A1-5) (ZNF2, Accession NM_021088) is another VGAM1335 host target gene. ZNF2 BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF2 BINDING SITE, designated SEQ ID:22068, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47331] Another function of VGAM1335 is therefore inhibition of Zinc Finger Protein 2 (A1-5) (ZNF2, Accession NM_021088). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF2. Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191) is another VGAM1335 host target gene. C1orf22 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf22 BINDING SITE, designated SEQ ID:24843, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47332] Another function of VGAM1335 is therefore inhibition of Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf22. Cyclin M1 (CNNM1, Accession NM_020348) is another VGAM1335 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21612, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47333] Another function of VGAM1335 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM_020348). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. FLJ10619 (Accession NM_018156) is another VGAM1335 host target gene. FLJ10619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10619, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10619 BINDING SITE, designated SEQ ID:19970, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47334] Another function of VGAM1335 is therefore inhibition of FLJ10619 (Accession NM_018156). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10619. FLJ20986 (Accession NM_024524) is another VGAM1335 host target gene. FLJ20986 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20986 BINDING SITE, designated SEQ ID:23729, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47335] Another function of VGAM1335 is therefore inhibition of FLJ20986 (Accession NM_024524). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20986. KIAA0748 (Accession NM_014796) is another VGAM1335 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16702, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47336] Another function of VGAM1335 is therefore inhibition of KIAA0748 (Accession NM_014796). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. MDS028 (Accession NM_018463) is another VGAM1335 host target gene. MDS028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDS028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDS028 BINDING SITE, designated SEQ ID:20537, to the nucleotide

sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47337] Another function of VGAM1335 is therefore inhibition of MDS028 (Accession NM_018463). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDS028. Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007) is another VGAM1335 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34883, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47338] Another function of VGAM1335 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. SCYB5 (Accession NM_002994) is another VGAM1335 host target gene.

SCYB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYB5 BINDING SITE, designated SEQ ID:8885, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47339] Another function of VGAM1335 is therefore inhibition of SCYB5 (Accession NM_002994). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYB5. Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285) is another VGAM1335 host target gene. TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TP53INP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2, designated SEQ ID:27113 and SEQ ID:36122 respectively, to the nucleotide sequence of VGAM1335 RNA, herein

designated VGAM RNA, also designated SEQ ID:4046.

[47340] Another function of VGAM1335 is therefore inhibition of Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession NM_033285). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53INP1. LOC158798 (Accession XM_088671) is another VGAM1335 host target gene. LOC158798 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158798 BINDING SITE, designated SEQ ID:39893, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47341] Another function of VGAM1335 is therefore inhibition of LOC158798 (Accession XM_088671). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158798. LOC196411 (Accession XM_113714) is another VGAM1335 host target gene. LOC196411 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC196411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196411 BINDING SITE, designated SEQ ID:42364, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47342] Another function of VGAM1335 is therefore inhibition of LOC196411 (Accession XM_113714). Accordingly, utilities of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196411. LOC90233 (Accession NM_138347) is another VGAM1335 host target gene. LOC90233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90233 BINDING SITE, designated SEQ ID:28745, to the nucleotide sequence of VGAM1335 RNA, herein designated VGAM RNA, also designated SEQ ID:4046.

[47343] Another function of VGAM1335 is therefore inhibition of LOC90233 (Accession NM_138347). Accordingly, utilities

of VGAM1335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90233. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1336 (VGAM1336) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47344] VGAM1336 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1336 was detected is described hereinabove with reference to Figs. 1-8.

[47345] VGAM1336 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox Virus. VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47346] VGAM1336 gene encodes a VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1336 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1336 precursor RNA is designated SEQ ID:1322, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1322 is located at position 83573 relative to the genome of Sheeppox Virus.

- [47347] VGAM1336 precursor RNA folds onto itself, forming VGAM1336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47348] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1336 folded precursor RNA into VGAM1336 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1336 RNA is designated SEQ ID:4047, and

is provided hereinbelow with reference to the sequence listing part.

[47349] VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1336 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[47350] VGAM1336 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1336 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1336 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47351] The complementary binding of VGAM1336 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1336 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1336 host target RNA into VGAM1336 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47352] It is appreciated that VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1336 host target genes. The mRNA of each one of this plurality of VGAM1336 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1336 RNA, herein designated VGAM RNA, and which when bound by VGAM1336 RNA causes inhibition of translation of respective one or more VGAM1336 host target proteins.

[47353] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1336 gene, herein designated VGAM GENE, on one or more VGAM1336 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47354] It is yet further appreciated that a function of VGAM1336 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGAM1336 correlate with, and may be deduced from, the identity of the host target genes which VGAM1336 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47355] Nucleotide sequences of the VGAM1336 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1336 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1336 are further described hereinbelow with reference to Table 1.

[47356] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1336 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1336 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47357] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1336 gene, herein designated VGAM is inhibition of expression of VGAM1336 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1336 correlate with, and may be deduced from, the identity of the target genes which VGAM1336 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47358] NCK-associated Protein 1 (NCKAP1, Accession NM_013436) is a VGAM1336 host target gene. NCKAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCKAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCKAP1 BINDING SITE, designated SEQ ID:15095, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47359] A function of VGAM1336 is therefore inhibition of NCK-associated Protein 1 (NCKAP1, Accession NM_013436). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCKAP1. ATPase, Class V, Type 10D

(ATP10D, Accession XM_054907) is another VGAM1336 host target gene. ATP10D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP10D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10D BINDING SITE, designated SEQ ID:36200, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47360] Another function of VGAM1336 is therefore inhibition of ATPase, Class V, Type 10D (ATP10D, Accession XM_054907). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10D. FLJ12085 (Accession NM_022771) is another VGAM1336 host target gene. FLJ12085 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12085 BINDING SITE, designated SEQ ID:23032, to the nucleotide sequence of VGAM1336

RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47361] Another function of VGAM1336 is therefore inhibition of FLJ12085 (Accession NM_022771). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12085. Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM_012090) is another VGAM1336 host target gene. MACF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MACF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MACF1 BINDING SITE, designated SEQ ID:14379, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47362] Another function of VGAM1336 is therefore inhibition of Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM_012090). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MACF1. SCLY (Accession NM_016510) is another VGAM1336 host target

gene. SCLY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCLY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCLY BINDING SITE, designated SEQ ID:18588, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47363] Another function of VGAM1336 is therefore inhibition of SCLY (Accession NM_016510). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCLY. LOC143879 (Accession XM_084666) is another VGAM1336 host target gene. LOC143879 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143879 BINDING SITE, designated SEQ ID:37658, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47364] Another function of VGAM1336 is therefore inhibition of

LOC143879 (Accession XM_084666). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143879. LOC197131 (Accession XM_113823) is another VGAM1336 host target gene. LOC197131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197131 BINDING SITE, designated SEQ ID:42447, to the nucleotide sequence of VGAM1336 RNA, herein designated VGAM RNA, also designated SEQ ID:4047.

[47365] Another function of VGAM1336 is therefore inhibition of LOC197131 (Accession XM_113823). Accordingly, utilities of VGAM1336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197131. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1337 (VGAM1337) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[47366] VGAM1337 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1337 was detected is described hereinabove with reference to Figs. 1–8.

[47367] VGAM1337 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Sheeppox Virus. VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47368] VGAM1337 gene encodes a VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1337 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1337 precursor RNA is designated SEQ ID:1323, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1323 is located at position 84667 relative to the genome of Sheeppox Virus.

[47369] VGAM1337 precursor RNA folds onto itself, forming VGAM1337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47370] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1337 folded precursor RNA into VGAM1337 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1337 RNA is designated SEQ ID:4048, and is provided hereinbelow with reference to the sequence listing part.

[47371] VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1337 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[47372] VGAM1337 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1337 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1337 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[47373] The complementary binding of VGAM1337 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1337 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1337 host target RNA into VGAM1337 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47374] It is appreciated that VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1337 host target genes. The mRNA of each one of this plurality of VGAM1337 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1337 RNA, herein designated VGAM RNA, and which when bound by VGAM1337 RNA causes inhibition of translation of respective one or more VGAM1337 host target proteins.

[47375] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1337 gene, herein designated VGAM GENE, on one

or more VGAM1337 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47376] It is yet further appreciated that a function of VGAM1337 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGAM1337 correlate with, and may be deduced from, the identity of the host target genes which VGAM1337 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47377] Nucleotide sequences of the VGAM1337 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1337 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1337 are further described hereinbelow with reference to Table 1.

[47378] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1337 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1337 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47379] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1337 gene, herein designated VGAM is inhibition of expression of VGAM1337 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1337 correlate with, and may be deduced from, the identity of the target genes which VGAM1337 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47380] RAN Binding Protein 2 (RANBP2, Accession NM_006267) is

a VGAM1337 host target gene. RANBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RANBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RANBP2 BINDING SITE, designated SEQ ID:12948, to the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, also designated SEQ ID:4048.

[47381] A function of VGAM1337 is therefore inhibition of RAN Binding Protein 2 (RANBP2, Accession NM_006267), a gene which is thought to control a variety of cellular functions through its interactions with other proteins. Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RANBP2. The function of RANBP2 has been established by previous studies. RAN (OMIM Ref. No. 601179) is a small GTP-binding protein of the RAS superfamily (see OMIM Ref. No. 190020) that is associated with the nuclear membrane and is thought to control a variety of cellular functions through its interactions with other proteins. Yokoyama et al. (1995) described a human cDNA for one such RAN-binding protein which they cloned us-

ing a 2-hybrid screen with RAN. The cDNA, designated RANBP2 (RAN-binding protein-2) by them, encodes a very large protein (3,224 amino acids) that was immunolocalized to the nuclear pore complex. The protein has a 700-residue leucine-rich domain at the amino end, 4 motifs in common with RANBP1 (OMIM Ref. No. 601180), 8 zinc finger motifs, and a C terminus related to cyclophilin (OMIM Ref. No. 123840). The authors showed that an antibody directed against RANBP2 inhibited nuclear import. Beddow et al. (1995) described a nearly identical partial cDNA which contains a motif of about 150 residues that stabilizes the GTP-bound state of RAN. A mutation in that domain markedly reduced RAN binding. The gene is also referred to as NUP358 (Wu et al., 1995). Pichler et al. (2002) showed that the nucleoporin RANBP2 has SUMO1 (OMIM Ref. No. 601912) E3-like activity. RANBP2 directly interacts with the E2 enzyme UBC9 (OMIM Ref. No. 601661) and strongly enhances SUMO1 transfer from UBC9 to the SUMO1 target SP100 (OMIM Ref. No. 604585). The E3-like activity is contained within a 33-kD domain of RANBP2 that lacks RING finger motifs and does not resemble PIAS (see OMIM Ref. No. 603566) family proteins. These findings placed sumoylation at the cytoplasmic fila-

ments of the nuclear pore complexes and suggested that, at least for some substrates, modification and nuclear import are linked events.

[47382] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47383] Beddow, A. L.; Richards, S. A.; Orem, N. R.; Macara, I. G. : The Ran/TC4 GTPase-binding domain: identification by expression cloning and characterization of a conserved sequence motif. *Proc. Nat. Acad. Sci.* 92: 3328–3332, 1995. ; and

[47384] Pichler, A.; Gast, A.; Seeler, J. S.; Dejean, A.; Melchior, F. : The nucleoporin RanBP2 has SUMO1 E3 ligase activity. *Cell* 108: 109–120, 2002.

[47385] Further studies establishing the function and utilities of RANBP2 are found in John Hopkins OMIM database record ID 601181, and in cited publications numbered 9499–9504 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp761D0614 (Accession XM_113634) is another VGAM1337 host target gene. DKFZp761D0614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D0614,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D0614 BINDING SITE, designated SEQ ID:42313, to the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, also designated SEQ ID:4048.

[47386] Another function of VGAM1337 is therefore inhibition of DKFZp761D0614 (Accession XM_113634). Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D0614. FLJ10546 (Accession XM_002989) is another VGAM1337 host target gene. FLJ10546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10546 BINDING SITE, designated SEQ ID:29910, to the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, also designated SEQ ID:4048.

[47387] Another function of VGAM1337 is therefore inhibition of FLJ10546 (Accession XM_002989). Accordingly, utilities of

VGAM1337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10546. FLJ23074 (Accession NM_025052) is another VGAM1337 host target gene. FLJ23074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23074 BINDING SITE, designated SEQ ID:24651, to the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, also designated SEQ ID:4048.

[47388] Another function of VGAM1337 is therefore inhibition of FLJ23074 (Accession NM_025052). Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23074. LOC123628 (Accession XM_063764) is another VGAM1337 host target gene. LOC123628 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC123628 BINDING SITE, designated SEQ ID:37254, to the nucleotide sequence of VGAM1337 RNA, herein designated VGAM RNA, also designated SEQ ID:4048.

[47389] Another function of VGAM1337 is therefore inhibition of LOC123628 (Accession XM_063764). Accordingly, utilities of VGAM1337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123628. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1338 (VGAM1338) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47390] VGAM1338 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1338 was detected is described hereinabove with reference to Figs. 1-8.

[47391] VGAM1338 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Variola Virus. VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47392] VGAM1338 gene encodes a VGAM1338 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1338 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1338 precursor RNA is designated SEQ ID:1324, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1324 is located at position 146622 relative to the genome of Variola Virus.

[47393] VGAM1338 precursor RNA folds onto itself, forming VGAM1338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47394] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1338 folded precursor RNA into VGAM1338 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1338 RNA is designated SEQ ID:4049, and is provided hereinbelow with reference to the sequence listing part.

[47395] VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1338 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47396] VGAM1338 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1338 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1338 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47397] The complementary binding of VGAM1338 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1338 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1338 host target RNA into VGAM1338 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47398] It is appreciated that VGAM1338 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1338 host target genes. The mRNA of each one of this plurality of VGAM1338 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1338 RNA, herein designated VGAM RNA, and which when bound by VGAM1338 RNA causes inhibition of translation of respective one or more VGAM1338 host target proteins.

[47399] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1338 gene, herein designated VGAM GENE, on one or more VGAM1338 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[47400] It is yet further appreciated that a function of VGAM1338 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1338 include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGAM1338 correlate with, and may be deduced from, the identity of the host target genes which VGAM1338 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47401] Nucleotide sequences of the VGAM1338 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1338 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1338 are further described hereinbelow with reference to Table 1.

[47402] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1338 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1338 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47403] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1338 gene, herein designated VGAM is inhibition of expression of VGAM1338 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1338 correlate with, and may be deduced from, the identity of the target genes which VGAM1338 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47404] FLJ13769 (Accession NM_025012) is a VGAM1338 host target gene. FLJ13769 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13769 BINDING SITE, designated SEQ ID:24595, to the nucleotide sequence of VGAM1338 RNA, herein designated VGAM RNA, also designated SEQ ID:4049.

[47405] A function of VGAM1338 is therefore inhibition of

FLJ13769 (Accession NM_025012). Accordingly, utilities of VGAM1338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13769. KIAA1958 (Accession XM_088566) is another VGAM1338 host target gene. KIAA1958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1958 BINDING SITE, designated SEQ ID:39830, to the nucleotide sequence of VGAM1338 RNA, herein designated VGAM RNA, also designated SEQ ID:4049.

[47406] Another function of VGAM1338 is therefore inhibition of KIAA1958 (Accession XM_088566). Accordingly, utilities of VGAM1338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1958. MGC26651 (Accession NM_144642) is another VGAM1338 host target gene. MGC26651 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC26651, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC26651 BINDING SITE, designated SEQ ID:29470, to the nucleotide sequence of VGAM1338 RNA, herein designated VGAM RNA, also designated SEQ ID:4049.

[47407] Another function of VGAM1338 is therefore inhibition of MGC26651 (Accession NM_144642). Accordingly, utilities of VGAM1338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26651. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1339 (VGAM1339) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47408] VGAM1339 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1339 was detected is described hereinabove with reference to Figs. 1-8.

[47409] VGAM1339 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[47410] VGAM1339 gene encodes a VGAM1339 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1339 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1339 precursor RNA is designated SEQ ID:1325, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1325 is located at position 245147 relative to the genome of Fowlpox Virus.

[47411] VGAM1339 precursor RNA folds onto itself, forming VGAM1339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47412] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1339 folded precursor RNA into VGAM1339 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1339 RNA is designated SEQ ID:4050, and is provided hereinbelow with reference to the sequence listing part.

[47413] VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1339 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47414] VGAM1339 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1339 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1339 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47415] The complementary binding of VGAM1339 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1339 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1339 host target RNA into VGAM1339 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47416] It is appreciated that VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1339 host target genes. The mRNA of each one of this plurality of VGAM1339 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1339 RNA, herein designated VGAM RNA, and which when bound by VGAM1339 RNA causes inhibition of translation of respective one or more VGAM1339 host target proteins.

[47417] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1339 gene, herein designated VGAM GENE, on one or more VGAM1339 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47418] It is yet further appreciated that a function of VGAM1339 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1339 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1339 correlate with, and may be deduced from, the identity of the host target genes which VGAM1339 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47419] Nucleotide sequences of the VGAM1339 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1339 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1339 are further described hereinbelow with reference to Table 1.

[47420] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1339 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1339 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47421] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1339 gene, herein designated VGAM is inhibition of expression of VGAM1339 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1339 correlate with, and may be deduced from, the identity of the target genes which VGAM1339 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47422] LOC199725 (Accession XM_117119) is a VGAM1339 host target gene. LOC199725 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199725 BINDING SITE, designated SEQ ID:43242, to the nucleotide sequence of VGAM1339 RNA, herein designated VGAM RNA, also designated SEQ ID:4050.

[47423] A function of VGAM1339 is therefore inhibition of LOC199725 (Accession XM_117119). Accordingly, utilities of VGAM1339 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199725. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1340 (VGAM1340) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47424] VGAM1340 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1340 was detected is described hereinabove with reference to Figs. 1-8.

[47425] VGAM1340 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Virus A. VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47426] VGAM1340 gene encodes a VGAM1340 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1340 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1340 precursor RNA is designated SEQ ID:1326, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1326 is located at position 7154 relative to the genome of Garlic Virus A.

- [47427] VGAM1340 precursor RNA folds onto itself, forming VGAM1340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47428] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1340 folded precursor RNA into VGAM1340 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1340 RNA is designated SEQ ID:4051, and is provided hereinbelow with reference to the sequence listing part.

[47429] VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1340 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[47430] VGAM1340 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1340 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1340 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47431] The complementary binding of VGAM1340 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1340 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1340 host target RNA into VGAM1340 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47432] It is appreciated that VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1340 host target genes. The mRNA of each one of this plurality of VGAM1340 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1340 RNA, herein designated VGAM RNA, and which when bound by VGAM1340 RNA causes inhibition of translation of respective one or more VGAM1340 host target proteins.

[47433] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1340 gene, herein designated VGAM GENE, on one or more VGAM1340 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47434] It is yet further appreciated that a function of VGAM1340 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of viral infection by Garlic Virus A. Specific functions, and accordingly utilities, of VGAM1340 correlate with, and may be deduced from, the identity of the host target genes which VGAM1340 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47435] Nucleotide sequences of the VGAM1340 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1340 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1340 are further described hereinbelow with reference to Table 1.

[47436] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1340 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1340 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[47437] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1340 gene, herein designated VGAM is inhibition of expression of VGAM1340 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1340 correlate with, and may be deduced from, the identity of the target genes which VGAM1340 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47438] Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2C (GRIN2C, Accession NM_000835) is a VGAM1340 host target gene. GRIN2C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GRIN2C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2C BINDING SITE, designated SEQ ID:6493, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47439] A function of VGAM1340 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2C (GRIN2C, Accession NM_000835), a gene which has effect

on CREB function, gene regulation, and neuronal survival. Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN2C. The function of GRIN2C has been established by previous studies. The NMDA receptors are 1 class of ionotropic glutamate receptors (see OMIM Ref. No. GRIN2D; 602717). By screening a human hippocampal cDNA library with a rat Nr2a (GRIN2A; 138253) cDNA, Lin et al. (1996) isolated cDNAs encoding GRIN2C, called NR2C by them. Northern blot analysis showed that the 4.4-kb GRIN2C mRNA was widely expressed in the brain, with the highest level of expression in the cerebellum; this transcript was also found in several other tissues. An additional, slightly larger, transcript was detected in the cerebellum. The sequence of the deduced 1,233-amino acid protein is 88% identical to those of rat and mouse Nr2c. Hydropathy analysis of GRIN2C predicted a large N terminus, 4 hydrophobic regions, and a large C terminus. Animal model experiments lend further support to the function of GRIN2C. Kadotani et al. (1996) showed that targeted disruption of the mouse Nmdar2c gene produced homozygous $-/-$ mice with no obvious deficiency. By gene targeting, Sprengel et al. (1998) gen-

erated mutant mice expressing the Nmdar2c gene without the large intracellular C-terminal domain. These mice were viable but exhibited deficits in motor coordination. The authors concluded that the observed phenotypes appear to reflect defective intracellular signaling.

[47440] It is appreciated that the abovementioned animal model for GRIN2C is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[47441] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47442] Kadotani, H.; Hirano, T.; Masugi, M.; Nakamura, K.; Nakao, K.; Katsuki, M.; Nakanishi, S. : Motor discoordination results from combined gene disruption of the NMDA receptor NR2A and NR2C subunits, but not from single disruption of the NR2A or NR2C subunit. J. Neurosci. 16: 7859–7867, 1996. ; and

[47443] Lin, Y. J.; Bovetto, S.; Carver, J. M.; Giordano, T. : Cloning of the cDNA for the human NMDA receptor NR2C subunit and its expression in the central nervous system and periphery. Mole.

[47444] Further studies establishing the function and utilities of

GRIN2C are found in John Hopkins OMIM database record ID 138254, and in cited publications numbered 3598, 11922, 1192 and 3599 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Period Homolog 2 (Drosophila) (PER2, Accession NM_022817) is another VGAM1340 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23092, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47445] Another function of VGAM1340 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM74.TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190) is another VGAM1340 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9184, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47446] Another function of VGAM1340 is therefore inhibition of TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAPBP. The function of TAPBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM122.Chromosome 20 Open Reading Frame 21 (C20orf21, Accession NM_017798) is another VGAM1340 host target gene. C20orf21 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by C20orf21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf21 BINDING SITE, designated SEQ ID:19440, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47447] Another function of VGAM1340 is therefore inhibition of Chromosome 20 Open Reading Frame 21 (C20orf21, Accession NM_017798). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf21.

FLJ10535 (Accession NM_018129) is another VGAM1340 host target gene. FLJ10535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10535 BINDING SITE, designated SEQ ID:19920, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47448] Another function of VGAM1340 is therefore inhibition of FLJ10535 (Accession NM_018129). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10535. FLJ10687 (Accession NM_018178) is another VGAM1340 host target gene. FLJ10687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10687 BINDING SITE, designated SEQ ID:20010, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47449] Another function of VGAM1340 is therefore inhibition of FLJ10687 (Accession NM_018178). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10687. KIAA0350 (Accession XM_028332) is another VGAM1340 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30672, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47450] Another function of VGAM1340 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. LEAP-2 (Accession NM_052971) is another VGAM1340 host target gene. LEAP-2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LEAP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEAP-2 BINDING SITE, designated SEQ ID:27543, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47451] Another function of VGAM1340 is therefore inhibition of LEAP-2 (Accession NM_052971). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEAP-2.

LOC148534 (Accession XM_086222) is another VGAM1340 host target gene. LOC148534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148534 BINDING SITE, designated SEQ ID:38547, to the nucleotide sequence of VGAM1340 RNA, herein designated VGAM RNA, also designated SEQ ID:4051.

[47452] Another function of VGAM1340 is therefore inhibition of LOC148534 (Accession XM_086222). Accordingly, utilities of VGAM1340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148534. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1341 (VGAM1341) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47453] VGAM1341 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1341 was detected is described hereinabove with reference to Figs. 1–8.

[47454] VGAM1341 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Virus A.

VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47455] VGAM1341 gene encodes a VGAM1341 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1341 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1341 precursor RNA is designated SEQ ID:1327, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1327 is located at position 6737 relative to the genome of Garlic Virus A.

[47456] VGAM1341 precursor RNA folds onto itself, forming VGAM1341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47457] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1341 folded precursor RNA into VGAM1341 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1341 RNA is designated SEQ ID:4052, and is provided hereinbelow with reference to the sequence listing part.

[47458] VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1341 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47459] VGAM1341 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1341 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1341 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47460] The complementary binding of VGAM1341 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1341 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1341 host target RNA into VGAM1341 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47461] It is appreciated that VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1341 host target genes. The mRNA of each one of this plurality of VGAM1341 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1341 RNA, herein designated VGAM RNA, and which when bound by VGAM1341 RNA causes inhibition of translation of respective one or more VGAM1341 host target proteins.

[47462] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1341 gene, herein designated VGAM GENE, on one or more VGAM1341 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47463] It is yet further appreciated that a function of VGAM1341 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of viral infection by Garlic Virus A. Specific functions, and accordingly utilities, of VGAM1341 correlate with, and may be deduced from, the identity of the host target genes which VGAM1341 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47464] Nucleotide sequences of the VGAM1341 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1341 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1341 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1341 are further described hereinbelow with reference to Table 1.

[47465] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1341 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1341 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47466] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1341 gene, herein designated VGAM is inhibition of expression of VGAM1341 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1341 correlate with, and may be deduced from, the identity of the target genes which VGAM1341 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47467] Aryl Hydrocarbon Receptor (AHR, Accession NM_001621) is a VGAM1341 host target gene. AHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AHR, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AHR BINDING SITE, designated SEQ ID:7333, to the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, also designated SEQ ID:4052.

[47468] A function of VGAM1341 is therefore inhibition of Aryl Hydrocarbon Receptor (AHR, Accession NM_001621), a gene which plays a role in modulating carcinogenesis through the induction of xenobiotic-metabolizing enzymes. Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AHR. The function of AHR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM368. Carbonic Anhydrase XII (CA12, Accession NM_001218) is another VGAM1341 host target gene. CA12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CA12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CA12 BINDING SITE,

designated SEQ ID:6879, to the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, also designated SEQ ID:4052.

[47469] Another function of VGAM1341 is therefore inhibition of Carbonic Anhydrase XII (CA12, Accession NM_001218), a gene which functions in cellular transport and metabolic processes. Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CA12. The function of CA12 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM508. Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM_006614) is another VGAM1341 host target gene. CHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHL1 BINDING SITE, designated SEQ ID:13394, to the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, also designated SEQ ID:4052.

[47470] Another function of VGAM1341 is therefore inhibition of Cell Adhesion Molecule with Homology to L1CAM (close homolog of L1) (CHL1, Accession NM_006614). Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHL1. KIAA1190 (Accession XM_048695) is another VGAM1341 host target gene. KIAA1190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1190 BINDING SITE, designated SEQ ID:35226, to the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, also designated SEQ ID:4052.

[47471] Another function of VGAM1341 is therefore inhibition of KIAA1190 (Accession XM_048695). Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1190. PRO1386 (Accession NM_031269) is another VGAM1341 host target gene. PRO1386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1386, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1386 BINDING SITE, designated SEQ ID:25286, to the nucleotide sequence of VGAM1341 RNA, herein designated VGAM RNA, also designated SEQ ID:4052.

[47472] Another function of VGAM1341 is therefore inhibition of PRO1386 (Accession NM_031269). Accordingly, utilities of VGAM1341 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1386. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1342 (VGAM1342) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47473] VGAM1342 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1342 was detected is described hereinabove with reference to Figs. 1-8.

[47474] VGAM1342 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Virus A.

VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47475] VGAM1342 gene encodes a VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1342 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1342 precursor RNA is designated SEQ ID:1328, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1328 is located at position 2936 relative to the genome of Garlic Virus A.

[47476] VGAM1342 precursor RNA folds onto itself, forming VGAM1342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47477] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1342 folded precursor RNA into VGAM1342 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM1342 RNA is designated SEQ ID:4053, and is provided hereinbelow with reference to the sequence listing part.

[47478] VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1342 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47479] VGAM1342 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1342 RNA is an accurate or a partial inversed–reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1342 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47480] The complementary binding of VGAM1342 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1342 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1342 host target RNA into VGAM1342 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47481] It is appreciated that VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1342 host target genes. The mRNA of each one of this plurality of VGAM1342 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1342 RNA, herein designated VGAM RNA, and which when bound by VGAM1342 RNA causes inhibition of translation of respective one or more VGAM1342 host target proteins.

[47482] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1342 gene, herein designated VGAM GENE, on one or more VGAM1342 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47483] It is yet further appreciated that a function of VGAM1342 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of viral infection by Garlic Virus A. Specific functions, and accordingly utilities, of VGAM1342 correlate with, and may be deduced from, the identity of the host target genes which VGAM1342 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47484] Nucleotide sequences of the VGAM1342 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1342 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1342 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1342 are further described hereinbelow with reference to Table 1.

[47485] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1342 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1342 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47486] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1342 gene, herein designated VGAM is inhibition of expression of VGAM1342 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1342 correlate with, and may be deduced from, the identity of the target genes which VGAM1342 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47487] Cadherin 5, Type 2, VE-cadherin (vascular epithelium) (CDH5, Accession NM_001795) is a VGAM1342 host target gene. CDH5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH5 BINDING SITE, designated SEQ ID:7548,

to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47488] A function of VGAM1342 is therefore inhibition of Cadherin 5, Type 2, VE-cadherin (vascular epithelium) (CDH5, Accession NM_001795), a gene which associates with alpha-catenin forming a link to the cytoskeleton. Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH5. The function of CDH5 has been established by previous studies. Cadherins are calcium-dependent adhesive proteins that mediate cell-to-cell interaction. Huber et al. (1996) noted that they constitute an expanding family of receptors involved in the structural and functional organization of cells in various tissues. Members of the family include epithelial cadherin (E-cadherin; 192090), neural cadherin (N-cadherin; 114020), placental cadherin (P-cadherin; 114021), muscle cadherin (M-cadherin; 114019), and vascular endothelial cadherin (VE-cadherin, or CDH5). They share a common domain structure and primary sequence homologies. Each cadherin type has a unique tissue-distribution pattern. In most of them, expression is not restricted to 1 cell type, and more than 1 cadherin type may be found at the sur-

face of a particular cell. The authors stated that endothelial cells have been shown to express N-cadherin, VE-cadherin, and to a lesser extent, P-cadherin. Among these, only VE-cadherin is expressed specifically in endothelial cells (Salomon et al., 1992). Furthermore, VE-cadherin is associated consistently with intercellular junctions, whereas N-cadherin remains diffuse on the cell membrane. In order to define the role of CDH5 and of its binding to beta-catenin (see OMIM Ref. No. 116806) in intracellular signaling, Carmeliet et al. (1999) generated mice that lacked a functional Cdh5 gene, that expressed a mutant Cdh5 gene lacking the beta-catenin-binding cytoplasmic tail, or that did not express detectable Cdh5 levels because of an intronic neomycin phosphotransferase (neo) gene. They found in all of these mice that deletion or truncation of the Cdh5 gene did not affect assembly of endothelial cells in vascular plexi, but did impair their subsequent remodeling and maturation, causing lethality at 9.5 days of gestation. Deficiency or truncation of Cdh5 induced endothelial apoptosis and abolished transmission of the endothelial survival signal by vascular endothelial growth factor A (VEGF; 192240) to AKT kinase (OMIM Ref. No. 164730) and BCL2 (OMIM Ref. No. 151430) via re-

duced complex formation with VEGF receptor-2 (OMIM Ref. No. 191306), beta-catenin, and phosphoinositide-3 kinase (see OMIM Ref. No. 171833). Thus, Carmeliet et al. (1999) concluded that CDH5/beta-catenin signaling controls endothelial survival.

[47489] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47490] Carmeliet, P.; Lampugnani, M.-G.; Moons, L.; Breviario, F.; Compernelle, V.; Bono, F.; Balconi, G.; Spagnuolo, R.; Oosthuysen, B.; Dewerchin, M.; Zanetti, A.; Angellilo, A.; and 11 others : Targeted deficiency of cytosolic truncation of the VE-cadherin gene in mice impairs VEGF-mediated endothelial survival and angiogenesis. Cell 98: 147-157, 1999. ; and

[47491] Huber, P.; Dalmon, J.; Engiles, J.; Breviario, F.; Gory, S.; Siracusa, L. D.; Buchberg, A. M.; Dejana, E. : Genomic structure and chromosomal mapping of the mouse VE-cadherin gene (Cdh5.

[47492] Further studies establishing the function and utilities of CDH5 are found in John Hopkins OMIM database record ID 601120, and in cited publications numbered 6362-636 and 11646 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is another VGAM1342 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28942, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47493] Another function of VGAM1342 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. RAB5A, Member RAS Oncogene Family (RAB5A, Accession NM_004162) is another VGAM1342 host target gene. RAB5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB5A BINDING SITE, designated SEQ ID:10371, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47494] Another function of VGAM1342 is therefore inhibition of RAB5A, Member RAS Oncogene Family (RAB5A, Accession NM_004162), a gene which is a rate-limiting component of the machinery regulating the kinetics of membrane traffic. Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB5A. The function of RAB5A has been established by previous studies. The *S. cerevisiae* YPT1 and SEC4 genes encode Ras-related GTP-binding proteins involved in the regulation of secretion. Mammalian cells express a large number of RAB proteins, GTP-binding proteins closely related to YPT1 and SEC4. By screening a human pheochromocytoma library with probes derived from the SEC4 gene and from various rat and human RAB cDNAs, Zahraoui et al. (1989) isolated cDNAs encoding RAB1 (OMIM Ref. No. 179508), RAB2 (OMIM Ref. No. 179509), RAB3A (OMIM Ref. No. 179490), RAB3B (OMIM Ref. No. 179510), RAB4 (OMIM Ref. No.

179511), RAB5, and RAB6 (OMIM Ref. No. 179513). Except for the closely related RAB3A and RAB3B, the deduced human RAB proteins share 32 to 50% homology. The predicted 214-amino acid RAB5 protein is 31% and 38% identical to SEC4 and YPT1, respectively. All 6 human RAB proteins tested bound GTP and exhibited GTPase activities in vitro. Northern blot analysis revealed that RAB5 was expressed as 2.7- and 2.8-kb mRNAs in a human fibroblast cell line. Bucci et al. (1992) demonstrated that RAB5 is a rate-limiting component of the machinery regulating the kinetics of membrane traffic in the early endocytic pathway. Stenmark et al. (1995) reported that rabaptin-5 (OMIM Ref. No. 603616) is an effector of RAB5 that transmits the signal of the active GTP-bound RAB5 conformation to the membrane docking and/or fusion apparatus. Xiao et al. (1997) found that tuberin (OMIM Ref. No. 191092) exhibits substantial GTPase-activating protein (GAP) activity towards RAB5, and that rabaptin-5 mediates the tuberin association with RAB5. The authors suggested that tuberin functions as a RAB5GAP in vivo to negatively regulate RAB5-GTP activity in endocytosis.

[47495] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [47496] Bucci, C.; Parton, R. G.; Mather, I. H.; Stunnenberg, H.; Simons, K.; Hoflack, B.; Zerial, M. : The small GTPase rab5 functions as a regulatory factor in the early endocytic pathway. Cell 70: 715–728, 1992. ; and
- [47497] Xiao, G.–H.; Shoarinejad, F.; Jin, F.; Golemis, E. A.; Yeung, R. S. : The tuberous sclerosis 2 gene product, tuberin, functions as a Rab5 GTPase activating protein (GAP) in modulating en.
- [47498] Further studies establishing the function and utilities of RAB5A are found in John Hopkins OMIM database record ID 179512, and in cited publications numbered 2542, 2539, 2543–254 and 2722 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp761K1423 (Accession NM_018422) is another VGAM1342 host target gene. DKFZp761K1423 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp761K1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761K1423 BINDING SITE, designated SEQ ID:20471, to the nucleotide sequence of

VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47499] Another function of VGAM1342 is therefore inhibition of DKFZp761K1423 (Accession NM_018422). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761K1423. Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571) is another VGAM1342 host target gene. HEYL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEYL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEYL BINDING SITE, designated SEQ ID:15929, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47500] Another function of VGAM1342 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEYL. KIAA0418 (Accession NM_014631) is another VGAM1342

host target gene. KIAA0418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0418 BINDING SITE, designated SEQ ID:15997, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47501] Another function of VGAM1342 is therefore inhibition of KIAA0418 (Accession NM_014631). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0418. KIAA1247 (Accession XM_030036) is another VGAM1342 host target gene. KIAA1247 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1247 BINDING SITE, designated SEQ ID:30989, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47502] Another function of VGAM1342 is therefore inhibition of KIAA1247 (Accession XM_030036). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1247. KIAA1701 (Accession XM_042087) is another VGAM1342 host target gene. KIAA1701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1701 BINDING SITE, designated SEQ ID:33684, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47503] Another function of VGAM1342 is therefore inhibition of KIAA1701 (Accession XM_042087). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1701. Mab-21-like 2 (C. elegans) (MAB21L2, Accession NM_006439) is another VGAM1342 host target gene. MAB21L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAB21L2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L2 BINDING SITE, designated SEQ ID:13149, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47504] Another function of VGAM1342 is therefore inhibition of Mab-21-like 2 (*C. elegans*) (MAB21L2, Accession NM_006439). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L2. MDS028 (Accession NM_018463) is another VGAM1342 host target gene. MDS028 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDS028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDS028 BINDING SITE, designated SEQ ID:20534, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47505] Another function of VGAM1342 is therefore inhibition of MDS028 (Accession NM_018463). Accordingly, utilities of

VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDS028. PRO2012 (Accession NM_018614) is another VGAM1342 host target gene. PRO2012 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2012 BINDING SITE, designated SEQ ID:20681, to the nucleotide sequence of VGAM1342 RNA, herein designated VGAM RNA, also designated SEQ ID:4053.

[47506] Another function of VGAM1342 is therefore inhibition of PRO2012 (Accession NM_018614). Accordingly, utilities of VGAM1342 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2012. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1343 (VGAM1343) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47507] VGAM1343 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1343 was detected is described hereinabove with reference to Figs. 1–8.

[47508] VGAM1343 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Garlic Virus A. VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47509] VGAM1343 gene encodes a VGAM1343 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1343 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1343 precursor RNA is designated SEQ ID:1329, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1329 is located at position 1501 relative to the genome of Garlic Virus A.

[47510] VGAM1343 precursor RNA folds onto itself, forming VGAM1343 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47511] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1343 folded precursor RNA into VGAM1343 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1343 RNA is designated SEQ ID:4054, and is provided hereinbelow with reference to the sequence listing part.

[47512] VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1343 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[47513] VGAM1343 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1343 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1343 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47514] The complementary binding of VGAM1343 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1343 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1343 host target RNA into VGAM1343 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47515] It is appreciated that VGAM1343 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1343 host target genes. The mRNA of each one of this plurality of VGAM1343 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1343 RNA, herein designated VGAM RNA, and which when bound by VGAM1343 RNA causes inhibition of translation of respective one or more VGAM1343 host target proteins.

[47516] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1343 gene, herein designated VGAM GENE, on one or more VGAM1343 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47517] It is yet further appreciated that a function of VGAM1343 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1343 include diagnosis, prevention and treatment of viral infection by Garlic Virus A. Specific functions, and accordingly utilities, of VGAM1343 correlate with, and may be deduced from, the identity of the host target genes which VGAM1343 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47518] Nucleotide sequences of the VGAM1343 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1343 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1343 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1343 are further
described hereinbelow with reference to Table 1.

[47519] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1343 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1343 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[47520] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1343 gene, herein designated VGAM is
inhibition of expression of VGAM1343 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1343 correlate with, and may be deduced
from, the identity of the target genes which VGAM1343
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[47521] CD22 Antigen (CD22, Accession NM_001771) is a
VGAM1343 host target gene. CD22 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by CD22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD22 BINDING SITE, designated SEQ ID:7531, to the nucleotide sequence of VGAM1343 RNA, herein designated VGAM RNA, also designated SEQ ID:4054.

[47522] A function of VGAM1343 is therefore inhibition of CD22 Antigen (CD22, Accession NM_001771), a gene which is an antigen expressed specifically in B lymphocytes (Cd22 antigen) and may act in cell-cell interactions. Accordingly, utilities of VGAM1343 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD22. The function of CD22 has been established by previous studies. Nonhuman mammalian cells express N-acetylneuraminic acid (OMIM Ref. No. Neu5Ac) and N-glycolylneuraminic acid (OMIM Ref. No. Neu5Gc). Human cells contain only Neu5Ac because of an exon deletion/frameshift mutation in cytidine monophospho-sialic acid hydroxylase (CMAH; 603209), which converts Neu5Ac to Neu5Gc. Sialic acid-binding immunoglobulin-like lectins, or SIGLECs, such as CD22 (SIGLEC2), recognize sialic

acids. Brinkman–Van der Linden et al. (2000) showed that human SIGLEC1 (SN; 600751) strongly prefers Neu5Ac over Neu5Gc. Sequence analysis of SIGLEC2 cDNA found that while the chimpanzee sequence is 97% homologous to human, bonobo and gorilla are only 96% homologous, and the orangutan is only 93% homologous. Using regions of SIGLEC2 proteins from mouse, chimpanzee, orangutan, and human fused to the Fc region of human IgG, and flow cytometry analysis, Brinkman–Van der Linden et al. (2000) showed that all bound well to chimpanzee Epstein–Barr virus (EBV)–transformed B cells, which expressed high levels of Neu5Gc. Except for mouse, all bound well to human EBV–transformed B cells, which expressed high levels of Neu5Ac. Animal model experiments lend further support to the function of CD22. O'Keefe et al. (1996) made observations in mice with a targeted disruption of the CD22 gene indicating that CD22 is a negative regulator of antigen receptor signaling whose onset of expression at the mature B cell stage may serve to raise the antigen concentration threshold required for B cell triggering. Splenic B cells from CD22 knockout mice were found to be hyperresponsive to receptor signaling. Heightened calcium fluxes and cell proliferation were obtained at lower ligand con-

centrations. The mice gave augmented immune response, had an expanded peritoneal B-1 cell population, and contained increased serum titers of autoantibody.

[47523] It is appreciated that the abovementioned animal model for CD22 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[47524] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47525] O'Keefe, T. L.; Williams, G. T.; Davies, S. L.; Neuberger, M. S. : Hyperresponsive B cells in CD22-deficient mice. Science 274: 798-801, 1996. ; and

[47526] Brinkman-Van der Linden, E. C. M.; Sjoberg, E. R.; Juneja, L. R.; Crocker, P. R.; Varki, N.; Varki, A. : Loss of N-glycolylneuraminic acid in human evolution: implications for sialic aci.

[47527] Further studies establishing the function and utilities of CD22 are found in John Hopkins OMIM database record ID 107266, and in cited publications numbered 206-20 and 2959-209 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dachshund Homolog (Drosophila) (DACH, Accession

NM_080759) is another VGAM1343 host target gene.

DACH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DACH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DACH BINDING SITE, designated SEQ ID:28033, to the nucleotide sequence of VGAM1343 RNA, herein designated VGAM RNA, also designated SEQ ID:4054.

[47528] Another function of VGAM1343 is therefore inhibition of Dachshund Homolog (Drosophila) (DACH, Accession NM_080759), a gene which regulates early progenitor cell proliferation during retinogenesis and pituitary development . Accordingly, utilities of VGAM1343 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DACH. The function of DACH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM260. Heme Oxygenase (decycling) 1 (HMOX1, Accession NM_002133) is another VGAM1343 host target gene. HMOX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMOX1, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMOX1 BINDING SITE, designated SEQ ID:7908, to the nucleotide sequence of VGAM1343 RNA, herein designated VGAM RNA, also designated SEQ ID:4054.

[47529] Another function of VGAM1343 is therefore inhibition of Heme Oxygenase (decycling) 1 (HMOX1, Accession NM_002133). Accordingly, utilities of VGAM1343 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMOX1. PCCX2 (Accession XM_038352) is another VGAM1343 host target gene. PCCX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCCX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCCX2 BINDING SITE, designated SEQ ID:32821, to the nucleotide sequence of VGAM1343 RNA, herein designated VGAM RNA, also designated SEQ ID:4054.

[47530] Another function of VGAM1343 is therefore inhibition of PCCX2 (Accession XM_038352). Accordingly, utilities of

VGAM1343 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCCX2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1344 (VGAM1344) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47531] VGAM1344 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1344 was detected is described hereinabove with reference to Figs. 1–8.

[47532] VGAM1344 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Macaca Mulatta Rhadinovirus. VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47533] VGAM1344 gene encodes a VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1344 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1344 precursor RNA is desig-

nated SEQ ID:1330, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1330 is located at position 128312 relative to the genome of Macaca Mulatta Rhadinovirus.

- [47534] VGAM1344 precursor RNA folds onto itself, forming VGAM1344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47535] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1344 folded precursor RNA into VGAM1344 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1344 RNA is designated SEQ ID:4055, and is provided hereinbelow with reference to the sequence

listing part.

[47536] VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1344 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47537] VGAM1344 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1344 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1344 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47538] The complementary binding of VGAM1344 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1344 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1344 host target RNA into VGAM1344 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47539] It is appreciated that VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1344 host target genes. The mRNA of each one of this plurality of VGAM1344 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1344 RNA, herein designated VGAM

RNA, and which when bound by VGAM1344 RNA causes inhibition of translation of respective one or more VGAM1344 host target proteins.

[47540] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1344 gene, herein designated VGAM GENE, on one or more VGAM1344 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47541] It is yet further appreciated that a function of VGAM1344 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1344 include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGAM1344 correlate with, and may be deduced from, the identity of the host target genes which VGAM1344 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47542] Nucleotide sequences of the VGAM1344 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1344 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1344 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1344 are further described hereinbelow with reference to Table 1.

[47543] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1344 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1344 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47544] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1344 gene, herein designated VGAM is

inhibition of expression of VGAM1344 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1344 correlate with, and may be deduced from, the identity of the target genes which VGAM1344 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47545] MOT8 (Accession NM_018836) is a VGAM1344 host target gene. MOT8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOT8 BINDING SITE, designated SEQ ID:20825, to the nucleotide sequence of VGAM1344 RNA, herein designated VGAM RNA, also designated SEQ ID:4055.

[47546] A function of VGAM1344 is therefore inhibition of MOT8 (Accession NM_018836). Accordingly, utilities of VGAM1344 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOT8. Toll-like Receptor 10 (TLR10, Accession NM_030956) is another VGAM1344 host target gene. TLR10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by TLR10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TLR10 BINDING SITE, designated SEQ ID:25229, to the nucleotide sequence of VGAM1344 RNA, herein designated VGAM RNA, also designated SEQ ID:4055.

[47547] Another function of VGAM1344 is therefore inhibition of Toll-like Receptor 10 (TLR10, Accession NM_030956). Accordingly, utilities of VGAM1344 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TLR10. YAP (Accession NM_139121) is another VGAM1344 host target gene. YAP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by YAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YAP BINDING SITE, designated SEQ ID:29153, to the nucleotide sequence of VGAM1344 RNA, herein designated VGAM RNA, also designated SEQ ID:4055.

[47548] Another function of VGAM1344 is therefore inhibition of YAP (Accession NM_139121). Accordingly, utilities of

VGAM1344 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1345 (VGAM1345) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47549] VGAM1345 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1345 was detected is described hereinabove with reference to Figs. 1–8.

[47550] VGAM1345 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Herpesvirus 1. VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47551] VGAM1345 gene encodes a VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1345 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1345 precursor RNA is desig-

nated SEQ ID:1331, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1331 is located at position 123564 relative to the genome of Bovine Herpesvirus 1.

- [47552] VGAM1345 precursor RNA folds onto itself, forming VGAM1345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47553] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1345 folded precursor RNA into VGAM1345 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1345 RNA is designated SEQ ID:4056, and is provided hereinbelow with reference to the sequence

listing part.

[47554] VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1345 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47555] VGAM1345 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1345 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1345 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47556] The complementary binding of VGAM1345 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1345 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1345 host target RNA into VGAM1345 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47557] It is appreciated that VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1345 host target genes. The mRNA of each one of this plurality of VGAM1345 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1345 RNA, herein designated VGAM

RNA, and which when bound by VGAM1345 RNA causes inhibition of translation of respective one or more VGAM1345 host target proteins.

[47558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1345 gene, herein designated VGAM GENE, on one or more VGAM1345 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47559] It is yet further appreciated that a function of VGAM1345 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1345 include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1345 correlate with, and may be deduced from, the identity of the host target genes which VGAM1345 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47560] Nucleotide sequences of the VGAM1345 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1345 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1345 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1345 are further described hereinbelow with reference to Table 1.

[47561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1345 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1345 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47562] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1345 gene, herein designated VGAM is

inhibition of expression of VGAM1345 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1345 correlate with, and may be deduced from, the identity of the target genes which VGAM1345 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47563] V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_007313) is a VGAM1345 host target gene. ABL1 BINDING SITE1 and ABL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABL1 BINDING SITE1 and ABL1 BINDING SITE2, designated SEQ ID:14228 and SEQ ID:11640 respectively, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47564] A function of VGAM1345 is therefore inhibition of V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_007313). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABL1.

Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_138565) is another VGAM1345 host target gene. EMS1 BINDING SITE1 and EMS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EMS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMS1 BINDING SITE1 and EMS1 BINDING SITE2, designated SEQ ID:28866 and SEQ ID:11735 respectively, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47565] Another function of VGAM1345 is therefore inhibition of Ems1 Sequence (mammary tumor and squamous cell carcinoma-associated (p80/85 src substrate) (EMS1, Accession NM_138565), a gene which may contribute to the organization of cell structure. in transformed cells may contribute to cellular growth regulation and transformation. Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMS1. The function of EMS1 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM497.PACE (Accession NM_002569) is another VGAM1345 host target gene. PACE BINDING SITE1 and PACE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PACE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE BINDING SITE1 and PACE BINDING SITE2, designated SEQ ID:8423 and SEQ ID:8425 respectively, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47566] Another function of VGAM1345 is therefore inhibition of PACE (Accession NM_002569), a gene which processes pro-parathyroid hormone, pro-transforming growth factor beta. Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE. The function of PACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM151.Syntaxin Binding Protein 1 (STXBP1, Accession NM_003165) is an-

other VGAM1345 host target gene. STXBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STXBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STXBP1 BINDING SITE, designated SEQ ID:9144, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47567] Another function of VGAM1345 is therefore inhibition of Syntaxin Binding Protein 1 (STXBP1, Accession NM_003165), a gene which may play a role in determining the specificity of intracellular fusion reactions. Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STXBP1. The function of STXBP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM708.Reserved (C8orf13, Accession XM_088377) is another VGAM1345 host target gene. C8orf13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf13, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf13 BINDING SITE, designated SEQ ID:39658, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47568] Another function of VGAM1345 is therefore inhibition of Reserved (C8orf13, Accession XM_088377). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf13. FLJ12442 (Accession NM_022908) is another VGAM1345 host target gene. FLJ12442 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12442 BINDING SITE, designated SEQ ID:23209, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47569] Another function of VGAM1345 is therefore inhibition of FLJ12442 (Accession NM_022908). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12442. FLJ21032 (Accession NM_024906) is another VGAM1345 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24396, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47570] Another function of VGAM1345 is therefore inhibition of FLJ21032 (Accession NM_024906). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ21432 (Accession NM_024551) is another VGAM1345 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23770, to the nucleotide

sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47571] Another function of VGAM1345 is therefore inhibition of FLJ21432 (Accession NM_024551). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. JM4 (Accession NM_007213) is another VGAM1345 host target gene. JM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JM4 BINDING SITE, designated SEQ ID:14078, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47572] Another function of VGAM1345 is therefore inhibition of JM4 (Accession NM_007213). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JM4. KIAA0984 (Accession XM_037557) is another VGAM1345 host target gene. KIAA0984 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by KIAA0984, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0984 BINDING SITE, designated SEQ ID:32643, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47573] Another function of VGAM1345 is therefore inhibition of KIAA0984 (Accession XM_037557). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0984. KIAA1463 (Accession XM_051160) is another VGAM1345 host target gene. KIAA1463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1463 BINDING SITE, designated SEQ ID:35769, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47574] Another function of VGAM1345 is therefore inhibition of KIAA1463 (Accession XM_051160). Accordingly, utilities

of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1463. KIAA1706 (Accession XM_166595) is another VGAM1345 host target gene. KIAA1706 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1706 BINDING SITE, designated SEQ ID:44575, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47575] Another function of VGAM1345 is therefore inhibition of KIAA1706 (Accession XM_166595). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1706. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1345 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of LASP1 BINDING SITE, designated SEQ ID:12792, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47576] Another function of VGAM1345 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. MGC16063 (Accession NM_053047) is another VGAM1345 host target gene. MGC16063 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16063 BINDING SITE, designated SEQ ID:27591, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47577] Another function of VGAM1345 is therefore inhibition of MGC16063 (Accession NM_053047). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC16063. MGC2474 (Accession NM_023931) is another VGAM1345 host target gene. MGC2474 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2474 BINDING SITE, designated SEQ ID:23421, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47578] Another function of VGAM1345 is therefore inhibition of MGC2474 (Accession NM_023931). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2474. Osteomodulin (OMD, Accession NM_005014) is another VGAM1345 host target gene. OMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OMD BINDING SITE, designated SEQ ID:11456, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA,

also designated SEQ ID:4056.

[47579] Another function of VGAM1345 is therefore inhibition of Osteomodulin (OMD, Accession NM_005014). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OMD. P37NB (Accession NM_005824) is another VGAM1345 host target gene. P37NB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P37NB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P37NB BINDING SITE, designated SEQ ID:12435, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47580] Another function of VGAM1345 is therefore inhibition of P37NB (Accession NM_005824). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P37NB. Period Homolog 3 (Drosophila) (PER3, Accession NM_016831) is another VGAM1345 host target gene. PER3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER3, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER3 BINDING SITE, designated SEQ ID:18822, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47581] Another function of VGAM1345 is therefore inhibition of Period Homolog 3 (Drosophila) (PER3, Accession NM_016831). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER3. T2BP (Accession XM_046111) is another VGAM1345 host target gene. T2BP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by T2BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of T2BP BINDING SITE, designated SEQ ID:34683, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47582] Another function of VGAM1345 is therefore inhibition of T2BP (Accession XM_046111). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with T2BP. Transducer of ERBB2, 2 (TOB2, Accession XM_170995) is another VGAM1345 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45766, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47583] Another function of VGAM1345 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM_170995). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. LOC120939 (Accession XM_073688) is another VGAM1345 host target gene. LOC120939 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120939 BINDING SITE, desig-

nated SEQ ID:37516, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47584] Another function of VGAM1345 is therefore inhibition of LOC120939 (Accession XM_073688). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120939. LOC128989 (Accession XM_059310) is another VGAM1345 host target gene. LOC128989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36941, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47585] Another function of VGAM1345 is therefore inhibition of LOC128989 (Accession XM_059310). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128989. LOC148085 (Accession XM_097388) is another VGAM1345 host target gene. LOC148085 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148085 BINDING SITE, designated SEQ ID:40868, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47586] Another function of VGAM1345 is therefore inhibition of LOC148085 (Accession XM_097388). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148085. LOC220776 (Accession XM_043388) is another VGAM1345 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33930, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47587] Another function of VGAM1345 is therefore inhibition of

LOC220776 (Accession XM_043388). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC221042 (Accession XM_167669) is another VGAM1345 host target gene. LOC221042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221042 BINDING SITE, designated SEQ ID:44752, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47588] Another function of VGAM1345 is therefore inhibition of LOC221042 (Accession XM_167669). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221042. LOC256905 (Accession XM_173031) is another VGAM1345 host target gene. LOC256905 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256905, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC256905 BINDING SITE, designated SEQ ID:46296, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47589] Another function of VGAM1345 is therefore inhibition of LOC256905 (Accession XM_173031). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256905. LOC93380 (Accession XM_051020) is another VGAM1345 host target gene. LOC93380 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93380 BINDING SITE, designated SEQ ID:35728, to the nucleotide sequence of VGAM1345 RNA, herein designated VGAM RNA, also designated SEQ ID:4056.

[47590] Another function of VGAM1345 is therefore inhibition of LOC93380 (Accession XM_051020). Accordingly, utilities of VGAM1345 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93380. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1346 (VGAM1346) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47591] VGAM1346 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1346 was detected is described hereinabove with reference to Figs. 1–8.

[47592] VGAM1346 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47593] VGAM1346 gene encodes a VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1346 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1346 precursor RNA is designated SEQ ID:1332, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1332 is located at position 256840 relative to the genome of Fowlpox Virus.

[47594] VGAM1346 precursor RNA folds onto itself, forming VGAM1346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47595] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1346 folded precursor RNA into VGAM1346 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1346 RNA is designated SEQ ID:4057, and is provided hereinbelow with reference to the sequence listing part.

[47596] VGAM1346 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1346 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47597] VGAM1346 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1346 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1346 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1346 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[47598] The complementary binding of VGAM1346 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1346 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1346 host target RNA into VGAM1346 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47599] It is appreciated that VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1346 host target genes. The mRNA of each one of this plurality of VGAM1346 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1346 RNA, herein designated VGAM RNA, and which when bound by VGAM1346 RNA causes inhibition of translation of respective one or more

VGAM1346 host target proteins.

[47600] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1346 gene, herein designated VGAM GENE, on one or more VGAM1346 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47601] It is yet further appreciated that a function of VGAM1346 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1346 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific

functions, and accordingly utilities, of VGAM1346 correlate with, and may be deduced from, the identity of the host target genes which VGAM1346 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47602] Nucleotide sequences of the VGAM1346 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1346 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1346 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1346 are further described hereinbelow with reference to Table 1.

[47603] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1346 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1346 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47604] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1346 gene, herein designated VGAM is inhibition of expression of VGAM1346 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1346 correlate with, and may be deduced from, the identity of the target genes which VGAM1346 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47605] ATPase, Ca++ Transporting, Cardiac Muscle, Slow Twitch 2 (ATP2A2, Accession NM_001681) is a VGAM1346 host target gene. ATP2A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP2A2 BINDING SITE, designated SEQ ID:7402, to the nucleotide sequence of VGAM1346 RNA, herein designated VGAM RNA, also designated SEQ ID:4057.

[47606] A function of VGAM1346 is therefore inhibition of ATPase, Ca++ Transporting, Cardiac Muscle, Slow Twitch 2 (ATP2A2, Accession NM_001681). Accordingly, utilities of VGAM1346 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP2A2. KIAA1674 (Accession XM_044065) is another VGAM1346 host target gene. KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34102, to the nucleotide sequence of VGAM1346 RNA, herein designated VGAM RNA, also designated SEQ ID:4057.

[47607] Another function of VGAM1346 is therefore inhibition of KIAA1674 (Accession XM_044065). Accordingly, utilities of VGAM1346 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1347 (VGAM1347) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47608] VGAM1347 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1347 was detected is described hereinabove with reference to Figs. 1-8.

[47609] VGAM1347 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Fowlpox Virus.

VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47610] VGAM1347 gene encodes a VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1347 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1347 precursor RNA is designated SEQ ID:1333, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1333 is located at position 251073 relative to the genome of Fowlpox Virus.

[47611] VGAM1347 precursor RNA folds onto itself, forming VGAM1347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47612] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1347 folded precursor RNA into VGAM1347 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1347 RNA is designated SEQ ID:4058, and is provided hereinbelow with reference to the sequence listing part.

[47613] VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1347 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47614] VGAM1347 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1347 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1347 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47615] The complementary binding of VGAM1347 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1347 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1347

host target RNA into VGAM1347 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47616] It is appreciated that VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1347 host target genes. The mRNA of each one of this plurality of VGAM1347 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1347 RNA, herein designated VGAM RNA, and which when bound by VGAM1347 RNA causes inhibition of translation of respective one or more VGAM1347 host target proteins.

[47617] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1347 gene, herein designated VGAM GENE, on one or more VGAM1347 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47618] It is yet further appreciated that a function of VGAM1347 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1347 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1347 correlate with, and may be deduced from, the identity of the host target genes which VGAM1347 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47619] Nucleotide sequences of the VGAM1347 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1347 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1347 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1347 are further

described hereinbelow with reference to Table 1.

[47620] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1347 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1347 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47621] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1347 gene, herein designated VGAM is inhibition of expression of VGAM1347 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1347 correlate with, and may be deduced from, the identity of the target genes which VGAM1347 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47622] Iduronate 2-sulfatase (Hunter syndrome) (IDS, Accession NM_000202) is a VGAM1347 host target gene. IDS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IDS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDS BIND-

ING SITE, designated SEQ ID:5698, to the nucleotide sequence of VGAM1347 RNA, herein designated VGAM RNA, also designated SEQ ID:4058.

[47623] A function of VGAM1347 is therefore inhibition of Iduronate 2-sulfatase (Hunter syndrome) (IDS, Accession NM_000202). Accordingly, utilities of VGAM1347 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDS. LOC200269 (Accession XM_114175) is another VGAM1347 host target gene. LOC200269 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200269, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200269 BINDING SITE, designated SEQ ID:42759, to the nucleotide sequence of VGAM1347 RNA, herein designated VGAM RNA, also designated SEQ ID:4058.

[47624] Another function of VGAM1347 is therefore inhibition of LOC200269 (Accession XM_114175). Accordingly, utilities of VGAM1347 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200269. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1348 (VGAM1348) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47625] VGAM1348 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1348 was detected is described hereinabove with reference to Figs. 1–8.

[47626] VGAM1348 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47627] VGAM1348 gene encodes a VGAM1348 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1348 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1348 precursor RNA is designated SEQ ID:1334, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1334 is located at position 254555 relative to the genome of Fowlpox Virus.

[47628] VGAM1348 precursor RNA folds onto itself, forming VGAM1348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47629] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1348 folded precursor RNA into VGAM1348 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1348 RNA is designated SEQ ID:4059, and is provided hereinbelow with reference to the sequence listing part.

[47630] VGAM1348 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1348 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47631] VGAM1348 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1348 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1348 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1348 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[47632] The complementary binding of VGAM1348 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1348 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1348 host target RNA into VGAM1348 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47633] It is appreciated that VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1348 host target genes. The mRNA of each one of this plurality of VGAM1348 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1348 RNA, herein designated VGAM RNA, and which when bound by VGAM1348 RNA causes inhibition of translation of respective one or more

VGAM1348 host target proteins.

[47634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1348 gene, herein designated VGAM GENE, on one or more VGAM1348 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47635] It is yet further appreciated that a function of VGAM1348 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific

functions, and accordingly utilities, of VGAM1348 correlate with, and may be deduced from, the identity of the host target genes which VGAM1348 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47636] Nucleotide sequences of the VGAM1348 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1348 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1348 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1348 are further described hereinbelow with reference to Table 1.

[47637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1348 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1348 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47638] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1348 gene, herein designated VGAM is inhibition of expression of VGAM1348 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1348 correlate with, and may be deduced from, the identity of the target genes which VGAM1348 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47639] Interferon Regulatory Factor 1 (IRF1, Accession XM_034862) is a VGAM1348 host target gene. IRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRF1 BINDING SITE, designated SEQ ID:32174, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47640] A function of VGAM1348 is therefore inhibition of Interferon Regulatory Factor 1 (IRF1, Accession XM_034862), a gene which specifically binds to the upstream regulatory region of type I IFN and IFN-inducible MHC class I genes. Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRF1. The function of IRF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM1264. Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355) is another VGAM1348 host target gene. MPP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP2 BINDING SITE, designated SEQ ID:30079, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47641] Another function of VGAM1348 is therefore inhibition of Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP2. Rhesus Blood Group, D Antigen (RHD, Accession NM_016225) is another VGAM1348 host target gene. RHD BINDING SITE1 and RHD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RHD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHD BINDING SITE1 and RHD BINDING SITE2, designated SEQ ID:18335 and SEQ ID:18215 respectively, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47642] Another function of VGAM1348 is therefore inhibition of Rhesus Blood Group, D Antigen (RHD, Accession NM_016225), a gene which Major antigen of the RH system. Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHD. The function of RHD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.FLJ10620 (Accession NM_018157) is another VGAM1348 host target gene. FLJ10620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10620 BINDING SITE, designated SEQ ID:19971, to the nucleotide sequence of VGAM1348

RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47643] Another function of VGAM1348 is therefore inhibition of FLJ10620 (Accession NM_018157). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10620. FLJ11753 (Accession NM_024659) is another VGAM1348 host target gene. FLJ11753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11753 BINDING SITE, designated SEQ ID:23962, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47644] Another function of VGAM1348 is therefore inhibition of FLJ11753 (Accession NM_024659). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11753. KIAA1100 (Accession NM_014901) is another VGAM1348 host target gene. KIAA1100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1100 BINDING SITE, designated SEQ ID:17086, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47645] Another function of VGAM1348 is therefore inhibition of KIAA1100 (Accession NM_014901). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1100. KIAA1199 (Accession XM_051860) is another VGAM1348 host target gene. KIAA1199 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1199, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1199 BINDING SITE, designated SEQ ID:35897, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47646] Another function of VGAM1348 is therefore inhibition of KIAA1199 (Accession XM_051860). Accordingly, utilities

of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1199. NCX (Accession NM_016170) is another VGAM1348 host target gene. NCX BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NCX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCX BINDING SITE, designated SEQ ID:18261, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47647] Another function of VGAM1348 is therefore inhibition of NCX (Accession NM_016170). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCX. Oligodendrocyte Transcription Factor 1 (OLIG1, Accession XM_170977) is another VGAM1348 host target gene. OLIG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OLIG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of OLIG1 BINDING SITE, designated SEQ ID:45752, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47648] Another function of VGAM1348 is therefore inhibition of Oligodendrocyte Transcription Factor 1 (OLIG1, Accession XM_170977). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLIG1. PP3501 (Accession NM_021731) is another VGAM1348 host target gene. PP3501 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP3501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP3501 BINDING SITE, designated SEQ ID:22329, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47649] Another function of VGAM1348 is therefore inhibition of PP3501 (Accession NM_021731). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PP3501. STIP-1 (Accession XM_045694) is another VGAM1348 host target gene. STIP-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STIP-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STIP-1 BINDING SITE, designated SEQ ID:34527, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47650] Another function of VGAM1348 is therefore inhibition of STIP-1 (Accession XM_045694). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STIP-1. YKT6 (Accession NM_006555) is another VGAM1348 host target gene. YKT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YKT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YKT6 BINDING SITE, designated SEQ ID:13318, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ

ID:4059.

[47651] Another function of VGAM1348 is therefore inhibition of YKT6 (Accession NM_006555). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YKT6. LOC145216 (Accession XM_096730) is another VGAM1348 host target gene. LOC145216 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145216 BINDING SITE, designated SEQ ID:40507, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47652] Another function of VGAM1348 is therefore inhibition of LOC145216 (Accession XM_096730). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145216. LOC146513 (Accession XM_097013) is another VGAM1348 host target gene. LOC146513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146513, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146513 BINDING SITE, designated SEQ ID:40708, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47653] Another function of VGAM1348 is therefore inhibition of LOC146513 (Accession XM_097013). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146513. LOC147081 (Accession XM_085696) is another VGAM1348 host target gene. LOC147081 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147081 BINDING SITE, designated SEQ ID:38288, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47654] Another function of VGAM1348 is therefore inhibition of LOC147081 (Accession XM_085696). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC147081. LOC257464 (Accession XM_116972) is another VGAM1348 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43162, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47655] Another function of VGAM1348 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC51194 (Accession NM_016338) is another VGAM1348 host target gene. LOC51194 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51194 BINDING SITE, designated SEQ ID:18459, to the

nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47656] Another function of VGAM1348 is therefore inhibition of LOC51194 (Accession NM_016338). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51194. LOC90190 (Accession XM_029758) is another VGAM1348 host target gene. LOC90190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90190 BINDING SITE, designated SEQ ID:30948, to the nucleotide sequence of VGAM1348 RNA, herein designated VGAM RNA, also designated SEQ ID:4059.

[47657] Another function of VGAM1348 is therefore inhibition of LOC90190 (Accession XM_029758). Accordingly, utilities of VGAM1348 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90190. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1349 (VGAM1349) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47658] VGAM1349 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1349 was detected is described hereinabove with reference to Figs. 1–8.

[47659] VGAM1349 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47660] VGAM1349 gene encodes a VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1349 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1349 precursor RNA is designated SEQ ID:1335, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1335 is located at position 252237 relative to the genome of Fowlpox Virus.

[47661] VGAM1349 precursor RNA folds onto itself, forming VGAM1349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47662] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1349 folded precursor RNA into VGAM1349 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1349 RNA is designated SEQ ID:4060, and is provided hereinbelow with reference to the sequence listing part.

[47663] VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1349 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1349 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47664] VGAM1349 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1349 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1349 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47665] The complementary binding of VGAM1349 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1349 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1349 host target RNA into VGAM1349 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47666] It is appreciated that VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1349 host target genes. The mRNA of each one of this plurality of VGAM1349 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1349 RNA, herein designated VGAM RNA, and which when bound by VGAM1349 RNA causes inhibition of translation of respective one or more VGAM1349 host target proteins.

[47667] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1349 gene, herein designated VGAM GENE, on one or more VGAM1349 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47668] It is yet further appreciated that a function of VGAM1349 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1349 correlate with, and may be deduced from, the identity of the

host target genes which VGAM1349 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47669] Nucleotide sequences of the VGAM1349 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1349 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1349 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1349 are further described hereinbelow with reference to Table 1.

[47670] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1349 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1349 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47671] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1349 gene, herein designated VGAM is inhibition of expression of VGAM1349 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1349 correlate with, and may be deduced from, the identity of the target genes which VGAM1349

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47672] DKFZP586D0623 (Accession XM_050418) is a VGAM1349 host target gene. DKFZP586D0623 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP586D0623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586D0623 BINDING SITE, designated SEQ ID:35626, to the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, also designated SEQ ID:4060.

[47673] A function of VGAM1349 is therefore inhibition of DKFZP586D0623 (Accession XM_050418). Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586D0623. Mitogen-activated Protein Kinase-activated Protein Kinase 3 (MAPKAPK3, Accession NM_004635) is another VGAM1349 host target gene. MAPKAPK3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAPKAPK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of MAPKAPK3 BINDING SITE, designated SEQ ID:11010, to the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, also designated SEQ ID:4060.

[47674] Another function of VGAM1349 is therefore inhibition of Mitogen-activated Protein Kinase-activated Protein Kinase 3 (MAPKAPK3, Accession NM_004635). Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPKAPK3. MGC10955 (Accession NM_032676) is another VGAM1349 host target gene. MGC10955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10955 BINDING SITE, designated SEQ ID:26398, to the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, also designated SEQ ID:4060.

[47675] Another function of VGAM1349 is therefore inhibition of MGC10955 (Accession NM_032676). Accordingly, utilities of VGAM1349 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC10955. Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255) is another VGAM1349 host target gene. MRPL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL10 BINDING SITE, designated SEQ ID:29768, to the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, also designated SEQ ID:4060.

[47676] Another function of VGAM1349 is therefore inhibition of Mitochondrial Ribosomal Protein L10 (MRPL10, Accession NM_145255). Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL10. LOC149578 (Accession XM_086592) is another VGAM1349 host target gene. LOC149578 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149578, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC149578 BINDING SITE, designated SEQ ID:38780, to the nucleotide sequence of VGAM1349 RNA, herein designated VGAM RNA, also designated SEQ ID:4060.

[47677] Another function of VGAM1349 is therefore inhibition of LOC149578 (Accession XM_086592). Accordingly, utilities of VGAM1349 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149578. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1350 (VGAM1350) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47678] VGAM1350 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1350 was detected is described hereinabove with reference to Figs. 1–8.

[47679] VGAM1350 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[47680] VGAM1350 gene encodes a VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1350 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1350 precursor RNA is designated SEQ ID:1336, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1336 is located at position 254693 relative to the genome of Fowlpox Virus.

[47681] VGAM1350 precursor RNA folds onto itself, forming VGAM1350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47682] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1350 folded precursor RNA into VGAM1350 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1350 RNA is designated SEQ ID:4061, and is provided hereinbelow with reference to the sequence listing part.

[47683] VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1350 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47684] VGAM1350 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1350 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1350 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47685] The complementary binding of VGAM1350 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1350 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1350 host target RNA into VGAM1350 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47686] It is appreciated that VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1350 host target genes. The mRNA of each one of this plurality of VGAM1350 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1350 RNA, herein designated VGAM RNA, and which when bound by VGAM1350 RNA causes inhibition of translation of respective one or more VGAM1350 host target proteins.

[47687] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1350 gene, herein designated VGAM GENE, on one or more VGAM1350 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47688] It is yet further appreciated that a function of VGAM1350 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1350 correlate with, and may be deduced from, the identity of the host target genes which VGAM1350 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47689] Nucleotide sequences of the VGAM1350 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1350 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1350 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1350 are further described hereinbelow with reference to Table 1.

[47690] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1350 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1350 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47691] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1350 gene, herein designated VGAM is inhibition of expression of VGAM1350 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1350 correlate with, and may be deduced from, the identity of the target genes which VGAM1350 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47692] Chloride Channel 3 (CLCN3, Accession NM_001829) is a VGAM1350 host target gene. CLCN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN3 BINDING SITE, designated SEQ ID:7568, to the nucleotide sequence of VGAM1350 RNA, herein designated VGAM RNA, also designated SEQ ID:4061.

[47693] A function of VGAM1350 is therefore inhibition of Chloride Channel 3 (CLCN3, Accession NM_001829), a gene which play a role in the neural cell function through regulation of membrane excitability. Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCN3. The function of CLCN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1332. Tripartite Motif-containing 14 (TRIM14, Accession NM_014788) is another VGAM1350 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM14 BINDING SITE, designated SEQ ID:16664, to the nucleotide sequence of VGAM1350 RNA, herein designated VGAM RNA, also designated SEQ ID:4061.

[47694] Another function of VGAM1350 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM_014788), a gene which is composed of 3 zinc-binding

domains and is involved in development and cell growth. Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM1350 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15346, to the nucleotide sequence of VGAM1350 RNA, herein designated VGAM RNA, also designated SEQ ID:4061.

[47695] Another function of VGAM1350 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. KIAA1431 (Accession XM_032055) is another VGAM1350 host target gene. KIAA1431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1431 BINDING SITE, designated SEQ ID:31549, to the nucleotide sequence of VGAM1350 RNA, herein designated VGAM RNA, also designated SEQ ID:4061.

[47696] Another function of VGAM1350 is therefore inhibition of KIAA1431 (Accession XM_032055). Accordingly, utilities of VGAM1350 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1431. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1351 (VGAM1351) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[47697] VGAM1351 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1351 was detected is described hereinabove with reference to Figs. 1-8.

[47698] VGAM1351 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47699] VGAM1351 gene encodes a VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1351 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1351 precursor RNA is designated SEQ ID:1337, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1337 is located at position 252589 relative to the genome of Fowlpox Virus.

[47700] VGAM1351 precursor RNA folds onto itself, forming VGAM1351 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47701] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1351 folded precursor RNA into VGAM1351 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1351 RNA is designated SEQ ID:4062, and is provided hereinbelow with reference to the sequence listing part.

[47702] VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1351 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47703] VGAM1351 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1351 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1351 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47704] The complementary binding of VGAM1351 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1351 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1351 host target RNA into VGAM1351 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47705] It is appreciated that VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1351 host target genes. The mRNA of each one of this plurality of VGAM1351 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1351 RNA, herein designated VGAM RNA, and which when bound by VGAM1351 RNA causes inhibition of translation of respective one or more VGAM1351 host target proteins.

[47706] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1351 gene, herein designated VGAM GENE, on one or more VGAM1351 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47707] It is yet further appreciated that a function of VGAM1351 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1351 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1351 correlate with, and may be deduced from, the identity of the host target genes which VGAM1351 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[47708] Nucleotide sequences of the VGAM1351 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1351 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1351 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1351 are further described hereinbelow with reference to Table 1.

[47709] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1351 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1351 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47710] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1351 gene, herein designated VGAM is inhibition of expression of VGAM1351 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1351 correlate with, and may be deduced from, the identity of the target genes which VGAM1351 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47711] ARPP-19 (Accession NM_006628) is a VGAM1351 host target gene. ARPP-19 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARPP-19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-19 BINDING SITE, designated SEQ ID:13421, to the nucleotide sequence of VGAM1351 RNA, herein designated VGAM RNA, also designated SEQ ID:4062.

[47712] A function of VGAM1351 is therefore inhibition of ARPP-19 (Accession NM_006628). Accordingly, utilities of VGAM1351 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-19. LOC113523 (Accession XM_054378) is another VGAM1351 host target gene. LOC113523 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC113523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113523 BINDING SITE, designated SEQ ID:36149, to the nucleotide sequence of VGAM1351 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4062.

[47713] Another function of VGAM1351 is therefore inhibition of LOC113523 (Accession XM_054378). Accordingly, utilities of VGAM1351 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113523. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1352 (VGAM1352) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47714] VGAM1352 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1352 was detected is described hereinabove with reference to Figs. 1–8.

[47715] VGAM1352 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47716] VGAM1352 gene encodes a VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1352 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1352 precursor RNA is designated SEQ ID:1338, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1338 is located at position 252917 relative to the genome of Fowlpox Virus.

- [47717] VGAM1352 precursor RNA folds onto itself, forming VGAM1352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47718] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1352 folded precursor RNA into VGAM1352 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1352 RNA is designated SEQ ID:4063, and is provided hereinbelow with reference to the sequence listing part.

[47719] VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1352 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47720] VGAM1352 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1352 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1352 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47721] The complementary binding of VGAM1352 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1352 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1352 host target RNA into VGAM1352 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47722] It is appreciated that VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1352 host target genes. The mRNA of

each one of this plurality of VGAM1352 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1352 RNA, herein designated VGAM RNA, and which when bound by VGAM1352 RNA causes inhibition of translation of respective one or more VGAM1352 host target proteins.

[47723] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1352 gene, herein designated VGAM GENE, on one or more VGAM1352 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[47724] It is yet further appreciated that a function of VGAM1352 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1352 correlate with, and may be deduced from, the identity of the host target genes which VGAM1352 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47725] Nucleotide sequences of the VGAM1352 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1352 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1352 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1352 are further described hereinbelow with reference to Table 1.

[47726] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1352 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1352 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47727] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1352 gene, herein designated VGAM is inhibition of expression of VGAM1352 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1352 correlate with, and may be deduced from, the identity of the target genes which VGAM1352 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47728] Homeo Box A7 (HOXA7, Accession NM_006896) is a VGAM1352 host target gene. HOXA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXA7 BINDING SITE, designated SEQ ID:13768, to the nucleotide sequence of VGAM1352 RNA, herein designated VGAM RNA, also designated SEQ ID:4063.

[47729] A function of VGAM1352 is therefore inhibition of Homeo Box A7 (HOXA7, Accession NM_006896), a gene which provides cells with specific positional identities on the an-

terior-posterior axis. Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXA7. The function of HOXA7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281) is another VGAM1352 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42838, to the nucleotide sequence of VGAM1352 RNA, herein designated VGAM RNA, also designated SEQ ID:4063.

[47730] Another function of VGAM1352 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281). Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A. DKFZp761N1114 (Accession XM_086327) is another

VGAM1352 host target gene. DKFZp761N1114 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp761N1114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N1114 BINDING SITE, designated SEQ ID:38603, to the nucleotide sequence of VGAM1352 RNA, herein designated VGAM RNA, also designated SEQ ID:4063.

[47731] Another function of VGAM1352 is therefore inhibition of DKFZp761N1114 (Accession XM_086327). Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761N1114. FLJ11040 (Accession NM_018307) is another VGAM1352 host target gene. FLJ11040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11040 BINDING SITE, designated SEQ ID:20297, to the nucleotide sequence of VGAM1352 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4063.

[47732] Another function of VGAM1352 is therefore inhibition of FLJ11040 (Accession NM_018307). Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11040. LOC199678 (Accession XM_117111) is another VGAM1352 host target gene. LOC199678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199678 BINDING SITE, designated SEQ ID:43226, to the nucleotide sequence of VGAM1352 RNA, herein designated VGAM RNA, also designated SEQ ID:4063.

[47733] Another function of VGAM1352 is therefore inhibition of LOC199678 (Accession XM_117111). Accordingly, utilities of VGAM1352 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199678. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1353 (VGAM1353) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47734] VGAM1353 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1353 was detected is described hereinabove with reference to Figs. 1–8.

[47735] VGAM1353 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Fowlpox Virus. VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47736] VGAM1353 gene encodes a VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1353 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1353 precursor RNA is designated SEQ ID:1339, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1339 is located at position 251158 relative to the genome of Fowlpox Virus.

[47737] VGAM1353 precursor RNA folds onto itself, forming

VGAM1353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47738] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1353 folded precursor RNA into VGAM1353 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1353 RNA is designated SEQ ID:4064, and is provided hereinbelow with reference to the sequence listing part.

[47739] VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1353 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47740] VGAM1353 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1353 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1353 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47741] The complementary binding of VGAM1353 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1353 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1353 host target RNA into VGAM1353 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47742] It is appreciated that VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1353 host target genes. The mRNA of each one of this plurality of VGAM1353 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1353 RNA, herein designated VGAM RNA, and which when bound by VGAM1353 RNA causes inhibition of translation of respective one or more VGAM1353 host target proteins.

[47743] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1353 gene, herein designated VGAM GENE, on one or more VGAM1353 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47744] It is yet further appreciated that a function of VGAM1353 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGAM1353 correlate with, and may be deduced from, the identity of the host target genes which VGAM1353 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[47745] Nucleotide sequences of the VGAM1353 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1353 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1353 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1353 are further described hereinbelow with reference to Table 1.

[47746] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1353 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1353 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47747] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1353 gene, herein designated VGAM is inhibition of expression of VGAM1353 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1353 correlate with, and may be deduced from, the identity of the target genes which VGAM1353 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[47748] Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM_017555) is a VGAM1353 host target gene. EGLN2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EGLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN2 BINDING SITE, designated SEQ ID:18993, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47749] A function of VGAM1353 is therefore inhibition of Egl Nine Homolog 2 (*C. elegans*) (EGLN2, Accession NM_017555), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN2. The function of EGLN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM432. BCL2-associated Athanogene 4 (BAG4, Accession NM_004874) is another VGAM1353 host target gene. BAG4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region

of mRNA encoded by BAG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG4 BINDING SITE, designated SEQ ID:11310, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47750] Another function of VGAM1353 is therefore inhibition of BCL2-associated Athanogene 4 (BAG4, Accession NM_004874). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG4. DKFZp761H079 (Accession NM_144996) is another VGAM1353 host target gene. DKFZp761H079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761H079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761H079 BINDING SITE, designated SEQ ID:29600, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47751] Another function of VGAM1353 is therefore inhibition of

DKFZp761H079 (Accession NM_144996). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761H079. KIAA0232 (Accession XM_052627) is another VGAM1353 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36040, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47752] Another function of VGAM1353 is therefore inhibition of KIAA0232 (Accession XM_052627). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. KIAA1116 (Accession NM_014892) is another VGAM1353 host target gene. KIAA1116 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1116 BINDING SITE, designated SEQ ID:17042, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47753] Another function of VGAM1353 is therefore inhibition of KIAA1116 (Accession NM_014892). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1116. KIAA1557 (Accession XM_028289) is another VGAM1353 host target gene. KIAA1557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1557 BINDING SITE, designated SEQ ID:30642, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47754] Another function of VGAM1353 is therefore inhibition of KIAA1557 (Accession XM_028289). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1557. LOC158549 (Accession XM_098963) is another

VGAM1353 host target gene. LOC158549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158549 BINDING SITE, designated SEQ ID:42013, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47755] Another function of VGAM1353 is therefore inhibition of LOC158549 (Accession XM_098963). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158549. LOC51212 (Accession NM_016380) is another VGAM1353 host target gene. LOC51212 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51212 BINDING SITE, designated SEQ ID:18519, to the nucleotide sequence of VGAM1353 RNA, herein designated VGAM RNA, also designated SEQ ID:4064.

[47756] Another function of VGAM1353 is therefore inhibition of LOC51212 (Accession NM_016380). Accordingly, utilities of VGAM1353 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51212. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1354 (VGAM1354) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47757] VGAM1354 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1354 was detected is described hereinabove with reference to Figs. 1–8.

[47758] VGAM1354 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47759] VGAM1354 gene encodes a VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1354 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1354 precursor RNA is designated SEQ ID:1340, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1340 is located at position 7412 relative to the genome of Triatoma Virus.

- [47760] VGAM1354 precursor RNA folds onto itself, forming VGAM1354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47761] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1354 folded precursor RNA into VGAM1354 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1354 RNA is designated SEQ ID:4065, and is provided hereinbelow with reference to the sequence listing part.

[47762] VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1354 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[47763] VGAM1354 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1354 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1354 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47764] The complementary binding of VGAM1354 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1354 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1354 host target RNA into VGAM1354 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47765] It is appreciated that VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1354 host target genes. The mRNA of each one of this plurality of VGAM1354 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1354 RNA, herein designated VGAM RNA, and which when bound by VGAM1354 RNA causes inhibition of translation of respective one or more VGAM1354 host target proteins.

[47766] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1354 gene, herein designated VGAM GENE, on one or more VGAM1354 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47767] It is yet further appreciated that a function of VGAM1354 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1354 correlate with, and may be deduced from, the identity of the host target genes which VGAM1354 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47768] Nucleotide sequences of the VGAM1354 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1354 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1354 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1354 are further described hereinbelow with reference to Table 1.

[47769] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1354 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1354 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[47770] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1354 gene, herein designated VGAM is inhibition of expression of VGAM1354 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1354 correlate with, and may be deduced from, the identity of the target genes which VGAM1354 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47771] Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512) is a VGAM1354 host target gene. GARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARP BINDING SITE, designated SEQ ID:12034, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47772] A function of VGAM1354 is therefore inhibition of Glycoprotein A Repetitions Predominant (GARP, Accession NM_005512). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with GARP. Growth Differentiation Factor 8 (GDF8, Accession NM_005259) is another VGAM1354 host target gene. GDF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GDF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GDF8 BINDING SITE, designated SEQ ID:11765, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47773] Another function of VGAM1354 is therefore inhibition of Growth Differentiation Factor 8 (GDF8, Accession NM_005259), a gene which acts specifically as a negative regulator of skeletal muscle growth. Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GDF8. The function of GDF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM386.LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM_005578) is another VGAM1354 host target gene. LPP

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPP BINDING SITE, designated SEQ ID:12104, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47774] Another function of VGAM1354 is therefore inhibition of LIM Domain Containing Preferred Translocation Partner In Lipoma (LPP, Accession NM_005578). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPP. RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884) is another VGAM1354 host target gene. RAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP1A BINDING SITE, designated SEQ ID:8793, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ

ID:4065.

[47775] Another function of VGAM1354 is therefore inhibition of RAP1A, Member of RAS Oncogene Family (RAP1A, Accession NM_002884), a gene which induces morphological reversion of a cell line transformed by a ras oncogene. Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP1A. The function of RAP1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM993.FLJ10052 (Accession NM_017982) is another VGAM1354 host target gene. FLJ10052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10052 BINDING SITE, designated SEQ ID:19713, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47776] Another function of VGAM1354 is therefore inhibition of FLJ10052 (Accession NM_017982). Accordingly, utilities of

VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10052. FLJ11730 (Accession NM_022756) is another VGAM1354 host target gene. FLJ11730 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11730, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11730 BINDING SITE, designated SEQ ID:22994, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47777] Another function of VGAM1354 is therefore inhibition of FLJ11730 (Accession NM_022756). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11730. FLJ21939 (Accession NM_022461) is another VGAM1354 host target gene. FLJ21939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21939

BINDING SITE, designated SEQ ID:22803, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47778] Another function of VGAM1354 is therefore inhibition of FLJ21939 (Accession NM_022461). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21939. FLJ23537 (Accession NM_024889) is another VGAM1354 host target gene. FLJ23537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23537 BINDING SITE, designated SEQ ID:24363, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47779] Another function of VGAM1354 is therefore inhibition of FLJ23537 (Accession NM_024889). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23537. KIAA0367 (Accession XM_041018) is another VGAM1354 host target gene. KIAA0367 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33421, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47780] Another function of VGAM1354 is therefore inhibition of KIAA0367 (Accession XM_041018). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA0555 (Accession NM_014790) is another VGAM1354 host target gene. KIAA0555 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0555, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0555 BINDING SITE, designated SEQ ID:16685, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47781] Another function of VGAM1354 is therefore inhibition of

KIAA0555 (Accession NM_014790). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0555. KIAA0594 (Accession XM_036117) is another VGAM1354 host target gene. KIAA0594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0594 BINDING SITE, designated SEQ ID:32388, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47782] Another function of VGAM1354 is therefore inhibition of KIAA0594 (Accession XM_036117). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0594. KIAA1691 (Accession XM_166523) is another VGAM1354 host target gene. KIAA1691 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1691, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1691 BINDING SITE, designated SEQ ID:44461, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47783] Another function of VGAM1354 is therefore inhibition of KIAA1691 (Accession XM_166523). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1691. MGC13159 (Accession NM_032927) is another VGAM1354 host target gene. MGC13159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13159 BINDING SITE, designated SEQ ID:26750, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47784] Another function of VGAM1354 is therefore inhibition of MGC13159 (Accession NM_032927). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13159. SCDGF-B (Accession NM_033135) is another

VGAM1354 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:26985 and SEQ ID:24883 respectively, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47785] Another function of VGAM1354 is therefore inhibition of SCDGF-B (Accession NM_033135). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCDGF-B. LOC152742 (Accession XM_098259) is another VGAM1354 host target gene. LOC152742 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152742 BINDING SITE, designated SEQ ID:41545, to

the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47786] Another function of VGAM1354 is therefore inhibition of LOC152742 (Accession XM_098259). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152742. LOC153163 (Accession XM_087612) is another VGAM1354 host target gene. LOC153163 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153163 BINDING SITE, designated SEQ ID:39363, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47787] Another function of VGAM1354 is therefore inhibition of LOC153163 (Accession XM_087612). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153163. LOC196453 (Accession XM_118365) is another VGAM1354 host target gene. LOC196453 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC196453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196453 BINDING SITE, designated SEQ ID:43577, to the nucleotide sequence of VGAM1354 RNA, herein designated VGAM RNA, also designated SEQ ID:4065.

[47788] Another function of VGAM1354 is therefore inhibition of LOC196453 (Accession XM_118365). Accordingly, utilities of VGAM1354 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196453. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1355 (VGAM1355) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47789] VGAM1355 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1355 was detected is described hereinabove with reference to Figs. 1-8.

[47790] VGAM1355 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Triatoma Virus.

VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47791] VGAM1355 gene encodes a VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1355 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1355 precursor RNA is designated SEQ ID:1341, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1341 is located at position 3387 relative to the genome of Triatoma Virus.

[47792] VGAM1355 precursor RNA folds onto itself, forming VGAM1355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47793] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1355 folded precursor RNA into VGAM1355 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1355 RNA is designated SEQ ID:4066, and is provided hereinbelow with reference to the sequence listing part.

[47794] VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1355 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47795] VGAM1355 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1355 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1355 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47796] The complementary binding of VGAM1355 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1355 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1355

host target RNA into VGAM1355 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47797] It is appreciated that VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1355 host target genes. The mRNA of each one of this plurality of VGAM1355 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1355 RNA, herein designated VGAM RNA, and which when bound by VGAM1355 RNA causes inhibition of translation of respective one or more VGAM1355 host target proteins.

[47798] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1355 gene, herein designated VGAM GENE, on one or more VGAM1355 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47799] It is yet further appreciated that a function of VGAM1355 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1355 correlate with, and may be deduced from, the identity of the host target genes which VGAM1355 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47800] Nucleotide sequences of the VGAM1355 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1355 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1355 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1355 are further

described hereinbelow with reference to Table 1.

[47801] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1355 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1355 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47802] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1355 gene, herein designated VGAM is inhibition of expression of VGAM1355 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1355 correlate with, and may be deduced from, the identity of the target genes which VGAM1355 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47803] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 2 (B3GALT2, Accession NM_003783) is a VGAM1355 host target gene. B3GALT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B3GALT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of B3GALT2 BINDING SITE, designated SEQ ID:9870, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47804] A function of VGAM1355 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 2 (B3GALT2, Accession NM_003783). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT2. UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778) is another VGAM1355 host target gene. B4GALT4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT4 BINDING SITE, designated SEQ ID:9860, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47805] Another function of VGAM1355 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase,

Polypeptide 4 (B4GALT4, Accession NM_003778). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT4. Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is another VGAM1355 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20738, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47806] Another function of VGAM1355 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM74.EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838) is another VGAM1355 host target gene. EGFL5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EGFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL5 BINDING SITE, designated SEQ ID:41882, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47807] Another function of VGAM1355 is therefore inhibition of EGF-like-domain, Multiple 5 (EGFL5, Accession XM_098838). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL5. Homeo Box B6 (HOXB6, Accession XM_008560) is another VGAM1355 host target gene. HOXB6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HOXB6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB6 BINDING SITE, des-

ignated SEQ ID:30087, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47808] Another function of VGAM1355 is therefore inhibition of Homeo Box B6 (HOXB6, Accession XM_008560), a gene which participates in establishing segmentation patterns and in determining segment identities. Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB6. The function of HOXB6 has been established by previous studies. See 142960. To understand better the developmental significance of the murine Hox-2.2 gene (the homolog of human HOXB6, also symbolized HOX2B), Kaur et al. (1992) generated gain-of-function mutants by using the chicken beta-actin promoter to drive ubiquitous expression in transgenic mice. The resulting Hox-2.2 misexpression produced early postnatal lethality as well as craniofacial and axial skeletal perturbations that included open eyes at birth, cleft palate, micrognathia, microtia, skull bone deficiencies, and structural and positional alterations in the vertebral column. Complete or partial absence of the supraoccipital bone and malformations of the exoccipital and the basioccipital

bones were observed. By fluorescence in situ hybridization, Apiou et al. (1996) mapped the HOXB gene cluster precisely to 17q21.3.

[47809] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47810] Apiou, F.; Flagiello, D.; Cillo, C.; Malfoy, B.; Poupon, M.-F.; Dutrillaux, B. : Fine mapping of human HOX gene clusters. *Cytogenet. Cell Genet.* 73: 114-115, 1996. ; and

[47811] Kaur, S.; Singh, G.; Stock, J. L.; Schreiner, C. M.; Kier, A. B.; Yager, K. L.; Mucenski, M. L.; Scott, W. J., Jr.; Potter, S. S. : Dominant mutation of the murine Hox-2.2 gene results.

[47812] Further studies establishing the function and utilities of HOXB6 are found in John Hopkins OMIM database record ID 142961, and in cited publications numbered 5223 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434G1415 (Accession NM_031292) is another VGAM1355 host target gene. DKFZP434G1415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434G1415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of DKFZP434G1415 BINDING SITE, designated SEQ ID:25314, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47813] Another function of VGAM1355 is therefore inhibition of DKFZP434G1415 (Accession NM_031292). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434G1415. KIAA1958 (Accession XM_088566) is another VGAM1355 host target gene. KIAA1958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1958 BINDING SITE, designated SEQ ID:39828, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47814] Another function of VGAM1355 is therefore inhibition of KIAA1958 (Accession XM_088566). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1958. LOC153163 (Accession XM_087612) is another

VGAM1355 host target gene. LOC153163 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153163 BINDING SITE, designated SEQ ID:39362, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47815] Another function of VGAM1355 is therefore inhibition of LOC153163 (Accession XM_087612). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153163. LOC200609 (Accession XM_117256) is another VGAM1355 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43325, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47816] Another function of VGAM1355 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC202266 (Accession XM_117373) is another VGAM1355 host target gene. LOC202266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202266 BINDING SITE, designated SEQ ID:43419, to the nucleotide sequence of VGAM1355 RNA, herein designated VGAM RNA, also designated SEQ ID:4066.

[47817] Another function of VGAM1355 is therefore inhibition of LOC202266 (Accession XM_117373). Accordingly, utilities of VGAM1355 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202266. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1356 (VGAM1356) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[47818] VGAM1356 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1356 was detected is described hereinabove with reference to Figs. 1–8.

[47819] VGAM1356 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47820] VGAM1356 gene encodes a VGAM1356 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1356 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1356 precursor RNA is designated SEQ ID:1342, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1342 is located at position 7993 relative to the genome of Triatoma Virus.

[47821] VGAM1356 precursor RNA folds onto itself, forming VGAM1356 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47822] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1356 folded precursor RNA into VGAM1356 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1356 RNA is designated SEQ ID:4067, and is provided hereinbelow with reference to the sequence listing part.

[47823] VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1356 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47824] VGAM1356 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1356 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1356 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47825] The complementary binding of VGAM1356 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1356 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1356 host target RNA into VGAM1356 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47826] It is appreciated that VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1356 host target genes. The mRNA of each one of this plurality of VGAM1356 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1356 RNA, herein designated VGAM RNA, and which when bound by VGAM1356 RNA causes inhibition of translation of respective one or more VGAM1356 host target proteins.

[47827] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1356 gene, herein designated VGAM GENE, on one or more VGAM1356 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47828] It is yet further appreciated that a function of VGAM1356 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1356 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1356 correlate with, and may be deduced from, the identity of the host target genes which VGAM1356 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[47829] Nucleotide sequences of the VGAM1356 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1356 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1356 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1356 are further described hereinbelow with reference to Table 1.

[47830] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1356 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1356 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47831] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1356 gene, herein designated VGAM is inhibition of expression of VGAM1356 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1356 correlate with, and may be deduced from, the identity of the target genes which VGAM1356 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47832] KIAA1348 (Accession XM_043826) is a VGAM1356 host target gene. KIAA1348 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1348 BINDING SITE, designated SEQ ID:34030, to the nucleotide sequence of VGAM1356 RNA, herein designated VGAM RNA, also designated SEQ ID:4067.

[47833] A function of VGAM1356 is therefore inhibition of KIAA1348 (Accession XM_043826). Accordingly, utilities of VGAM1356 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1348. RAB39, Member RAS Oncogene Family (RAB39, Accession XM_084662) is another VGAM1356 host target gene. RAB39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB39 BINDING SITE, designated SEQ ID:37645, to the nucleotide sequence of VGAM1356 RNA,

herein designated VGAM RNA, also designated SEQ ID:4067.

[47834] Another function of VGAM1356 is therefore inhibition of RAB39, Member RAS Oncogene Family (RAB39, Accession XM_084662). Accordingly, utilities of VGAM1356 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB39. LOC150630 (Accession XM_097931) is another VGAM1356 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41237, to the nucleotide sequence of VGAM1356 RNA, herein designated VGAM RNA, also designated SEQ ID:4067.

[47835] Another function of VGAM1356 is therefore inhibition of LOC150630 (Accession XM_097931). Accordingly, utilities of VGAM1356 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1357 (VGAM1357) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47836] VGAM1357 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1357 was detected is described hereinabove with reference to Figs. 1–8.

[47837] VGAM1357 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47838] VGAM1357 gene encodes a VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1357 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1357 precursor RNA is designated SEQ ID:1343, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1343 is located at position 7136 relative to the

genome of Triatoma Virus.

[47839] VGAM1357 precursor RNA folds onto itself, forming VGAM1357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47840] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1357 folded precursor RNA into VGAM1357 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1357 RNA is designated SEQ ID:4068, and is provided hereinbelow with reference to the sequence listing part.

[47841] VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1357 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47842] VGAM1357 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1357 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1357 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47843] The complementary binding of VGAM1357 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1357 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1357 host target RNA into VGAM1357 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47844] It is appreciated that VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1357 host target genes. The mRNA of each one of this plurality of VGAM1357 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1357 RNA, herein designated VGAM RNA, and which when bound by VGAM1357 RNA causes inhibition of translation of respective one or more VGAM1357 host target proteins.

[47845] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1357 gene, herein designated VGAM GENE, on one or more VGAM1357 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47846] It is yet further appreciated that a function of VGAM1357 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1357 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1357 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47847] Nucleotide sequences of the VGAM1357 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1357 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1357 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1357 are further described hereinbelow with reference to Table 1.

[47848] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1357 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1357 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47849] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1357 gene, herein designated VGAM is inhibition of expression of VGAM1357 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1357 correlate with, and may be deduced

from, the identity of the target genes which VGAM1357 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47850] 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187) is a VGAM1357 host target gene. OAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS3 BINDING SITE, designated SEQ ID:12863, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47851] A function of VGAM1357 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS3. The function of OAS3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM309. Chromosome 1 Open Reading Frame 9 (C1orf9, Accession NM_016227) is another VGAM1357 host target gene. C1orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf9 BINDING SITE, designated SEQ ID:18341, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47852] Another function of VGAM1357 is therefore inhibition of Chromosome 1 Open Reading Frame 9 (C1orf9, Accession NM_016227). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf9. ENDOFIN (Accession NM_014733) is another VGAM1357 host target gene. ENDOFIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENDOFIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENDOFIN BINDING SITE, designated SEQ

ID:16369, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47853] Another function of VGAM1357 is therefore inhibition of ENDOFIN (Accession NM_014733). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENDOFIN. FLJ10607 (Accession XM_085119) is another VGAM1357 host target gene. FLJ10607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10607 BINDING SITE, designated SEQ ID:37831, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47854] Another function of VGAM1357 is therefore inhibition of FLJ10607 (Accession XM_085119). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10607. KIAA0332 (Accession XM_031553) is another VGAM1357 host target gene. KIAA0332 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0332 BINDING SITE, designated SEQ ID:31424, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47855] Another function of VGAM1357 is therefore inhibition of KIAA0332 (Accession XM_031553). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0332. NBR2 (Accession NM_005821) is another VGAM1357 host target gene. NBR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBR2 BINDING SITE, designated SEQ ID:12422, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47856] Another function of VGAM1357 is therefore inhibition of

NBR2 (Accession NM_005821). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBR2. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM1357 host target gene. ZDHHC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18491, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47857] Another function of VGAM1357 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC128338 (Accession XM_059238) is another VGAM1357 host target gene. LOC128338 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128338, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128338 BINDING SITE, designated SEQ ID:36926, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47858] Another function of VGAM1357 is therefore inhibition of LOC128338 (Accession XM_059238). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128338. LOC253981 (Accession XM_171064) is another VGAM1357 host target gene. LOC253981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253981 BINDING SITE, designated SEQ ID:45869, to the nucleotide sequence of VGAM1357 RNA, herein designated VGAM RNA, also designated SEQ ID:4068.

[47859] Another function of VGAM1357 is therefore inhibition of LOC253981 (Accession XM_171064). Accordingly, utilities of VGAM1357 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253981. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1358 (VGAM1358) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47860] VGAM1358 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1358 was detected is described hereinabove with reference to Figs. 1–8.

[47861] VGAM1358 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47862] VGAM1358 gene encodes a VGAM1358 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1358 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1358 precursor RNA is desig-

nated SEQ ID:1344, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1344 is located at position 8558 relative to the genome of Triatoma Virus.

- [47863] VGAM1358 precursor RNA folds onto itself, forming VGAM1358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [47864] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1358 folded precursor RNA into VGAM1358 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1358 RNA is designated SEQ ID:4069, and is provided hereinbelow with reference to the sequence

listing part.

[47865] VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1358 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47866] VGAM1358 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1358 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1358 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47867] The complementary binding of VGAM1358 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1358 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1358 host target RNA into VGAM1358 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47868] It is appreciated that VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1358 host target genes. The mRNA of each one of this plurality of VGAM1358 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1358 RNA, herein designated VGAM

RNA, and which when bound by VGAM1358 RNA causes inhibition of translation of respective one or more VGAM1358 host target proteins.

[47869] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1358 gene, herein designated VGAM GENE, on one or more VGAM1358 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47870] It is yet further appreciated that a function of VGAM1358 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1358 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1358 correlate with, and may be deduced from, the identity of the host target genes which VGAM1358 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47871] Nucleotide sequences of the VGAM1358 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1358 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1358 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1358 are further described hereinbelow with reference to Table 1.

[47872] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1358 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1358 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47873] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1358 gene, herein designated VGAM is

inhibition of expression of VGAM1358 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1358 correlate with, and may be deduced from, the identity of the target genes which VGAM1358 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47874] Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is a VGAM1358 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10688, to the nucleotide sequence of VGAM1358 RNA, herein designated VGAM RNA, also designated SEQ ID:4069.

[47875] A function of VGAM1358 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM1358 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM57.FLJ10244 (Accession NM_018037) is another VGAM1358 host target gene. FLJ10244 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10244 BINDING SITE, designated SEQ ID:19778, to the nucleotide sequence of VGAM1358 RNA, herein designated VGAM RNA, also designated SEQ ID:4069.

[47876] Another function of VGAM1358 is therefore inhibition of FLJ10244 (Accession NM_018037). Accordingly, utilities of VGAM1358 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10244. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1359 (VGAM1359) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47877] VGAM1359 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1359 was detected is described hereinabove with reference to Figs. 1-8.

[47878] VGAM1359 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47879] VGAM1359 gene encodes a VGAM1359 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1359 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1359 precursor RNA is designated SEQ ID:1345, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1345 is located at position 2393 relative to the genome of Triatoma Virus.

[47880] VGAM1359 precursor RNA folds onto itself, forming VGAM1359 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47881] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1359 folded precursor RNA into VGAM1359 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1359 RNA is designated SEQ ID:4070, and is provided hereinbelow with reference to the sequence listing part.

[47882] VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1359 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[47883] VGAM1359 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1359 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1359 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47884] The complementary binding of VGAM1359 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1359 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1359 host target RNA into VGAM1359 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47885] It is appreciated that VGAM1359 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1359 host target genes. The mRNA of each one of this plurality of VGAM1359 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1359 RNA, herein designated VGAM RNA, and which when bound by VGAM1359 RNA causes inhibition of translation of respective one or more VGAM1359 host target proteins.

[47886] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1359 gene, herein designated VGAM GENE, on one or more VGAM1359 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47887] It is yet further appreciated that a function of VGAM1359 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1359 correlate with, and may be deduced from, the identity of the host target genes which VGAM1359 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47888] Nucleotide sequences of the VGAM1359 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1359 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1359 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1359 are further
described hereinbelow with reference to Table 1.

[47889] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1359 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1359 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[47890] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1359 gene, herein designated VGAM is
inhibition of expression of VGAM1359 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1359 correlate with, and may be deduced
from, the identity of the target genes which VGAM1359
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[47891] Microtubule-associated Protein, RP/EB Family, Member 1
(MAPRE1, Accession NM_012325) is a VGAM1359 host

target gene. MAPRE1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE1 BINDING SITE, designated SEQ ID:14709, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47892] A function of VGAM1359 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 1 (MAPRE1, Accession NM_012325). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE1. Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242) is another VGAM1359 host target gene. MBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBL2 BINDING SITE, designated SEQ ID:5765, to the nucleotide sequence of

VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47893] Another function of VGAM1359 is therefore inhibition of Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBL2. Polycystic Kidney Disease 2 (autosomal dominant) (PKD2, Accession XM_011124) is another VGAM1359 host target gene. PKD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKD2 BINDING SITE, designated SEQ ID:30178, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47894] Another function of VGAM1359 is therefore inhibition of Polycystic Kidney Disease 2 (autosomal dominant) (PKD2, Accession XM_011124). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKD2.

DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 33 (DDX33, Accession NM_020162) is another VGAM1359 host target gene. DDX33 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DDX33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX33 BINDING SITE, designated SEQ ID:21377, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47895] Another function of VGAM1359 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 33 (DDX33, Accession NM_020162). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX33. FLJ13491 (Accession NM_024623) is another VGAM1359 host target gene. FLJ13491 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13491, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13491 BINDING SITE,

designated SEQ ID:23889, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47896] Another function of VGAM1359 is therefore inhibition of FLJ13491 (Accession NM_024623). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13491. KIAA1915 (Accession XM_055481) is another VGAM1359 host target gene. KIAA1915 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1915 BINDING SITE, designated SEQ ID:36271, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47897] Another function of VGAM1359 is therefore inhibition of KIAA1915 (Accession XM_055481). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1915. NXP-2 (Accession XM_048706) is another VGAM1359 host target gene. NXP-2 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by NXP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXP-2 BINDING SITE, designated SEQ ID:35231, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47898] Another function of VGAM1359 is therefore inhibition of NXP-2 (Accession XM_048706). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXP-2. Zinc Finger Protein 33a (KOX 31) (ZNF33A, Accession XM_166119) is another VGAM1359 host target gene. ZNF33A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF33A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF33A BINDING SITE, designated SEQ ID:43902, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47899] Another function of VGAM1359 is therefore inhibition of Zinc Finger Protein 33a (K0X 31) (ZNF33A, Accession XM_166119). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF33A. LOC157226 (Accession XM_033876) is another VGAM1359 host target gene. LOC157226 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157226 BINDING SITE, designated SEQ ID:31977, to the nucleotide sequence of VGAM1359 RNA, herein designated VGAM RNA, also designated SEQ ID:4070.

[47900] Another function of VGAM1359 is therefore inhibition of LOC157226 (Accession XM_033876). Accordingly, utilities of VGAM1359 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157226. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1360 (VGAM1360) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47901] VGAM1360 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1360 was detected is described hereinabove with reference to Figs. 1–8.

[47902] VGAM1360 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Triatoma Virus. VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47903] VGAM1360 gene encodes a VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1360 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1360 precursor RNA is designated SEQ ID:1346, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1346 is located at position 6392 relative to the genome of Triatoma Virus.

[47904] VGAM1360 precursor RNA folds onto itself, forming

VGAM1360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47905] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1360 folded precursor RNA into VGAM1360 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1360 RNA is designated SEQ ID:4071, and is provided hereinbelow with reference to the sequence listing part.

[47906] VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1360 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47907] VGAM1360 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1360 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1360 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47908] The complementary binding of VGAM1360 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1360 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1360 host target RNA into VGAM1360 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47909] It is appreciated that VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1360 host target genes. The mRNA of each one of this plurality of VGAM1360 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1360 RNA, herein designated VGAM RNA, and which when bound by VGAM1360 RNA causes inhibition of translation of respective one or more VGAM1360 host target proteins.

[47910] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1360 gene, herein designated VGAM GENE, on one or more VGAM1360 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47911] It is yet further appreciated that a function of VGAM1360 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1360 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1360 correlate with, and may be deduced from, the identity of the host target genes which VGAM1360 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47912] Nucleotide sequences of the VGAM1360 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1360 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1360 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1360 are further described hereinbelow with reference to Table 1.

[47913] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1360 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1360 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47914] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1360 gene, herein designated VGAM is inhibition of expression of VGAM1360 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1360 correlate with, and may be deduced from, the identity of the target genes which VGAM1360 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47915] PART1 (Accession NM_016590) is a VGAM1360 host target gene. PART1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PART1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PART1 BINDING SITE, designated SEQ ID:18665, to the nucleotide sequence of VGAM1360 RNA, herein designated VGAM RNA, also designated SEQ ID:4071.

[47916] A function of VGAM1360 is therefore inhibition of PART1 (Accession NM_016590). Accordingly, utilities of VGAM1360 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PART1. Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM_133445) is another VGAM1360 host target gene. GRIN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN3A BINDING SITE, designated SEQ ID:28537, to the nucleotide sequence of VGAM1360 RNA, herein designated VGAM RNA, also designated SEQ ID:4071.

[47917] Another function of VGAM1360 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl-D-aspartate 3A (GRIN3A, Accession NM_133445). Accordingly, utilities of VGAM1360 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN3A. KIAA0218 (Accession NM_014760) is another VGAM1360 host target gene. KIAA0218 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0218 BINDING SITE, designated SEQ ID:16518, to the nucleotide sequence of VGAM1360 RNA, herein designated VGAM RNA, also designated SEQ ID:4071.

[47918] Another function of VGAM1360 is therefore inhibition of KIAA0218 (Accession NM_014760). Accordingly, utilities of VGAM1360 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0218. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1361 (VGAM1361) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47919] VGAM1361 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1361 was detected is described hereinabove with reference to Figs. 1-8.

[47920] VGAM1361 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Triatoma Virus.

VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47921] VGAM1361 gene encodes a VGAM1361 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1361 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1361 precursor RNA is designated SEQ ID:1347, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1347 is located at position 5836 relative to the genome of Triatoma Virus.

[47922] VGAM1361 precursor RNA folds onto itself, forming VGAM1361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47923] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1361 folded precursor RNA into VGAM1361 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1361 RNA is designated SEQ ID:4072, and is provided hereinbelow with reference to the sequence listing part.

[47924] VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1361 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47925] VGAM1361 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1361 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1361 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47926] The complementary binding of VGAM1361 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1361 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1361

host target RNA into VGAM1361 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47927] It is appreciated that VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1361 host target genes. The mRNA of each one of this plurality of VGAM1361 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1361 RNA, herein designated VGAM RNA, and which when bound by VGAM1361 RNA causes inhibition of translation of respective one or more VGAM1361 host target proteins.

[47928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1361 gene, herein designated VGAM GENE, on one or more VGAM1361 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47929] It is yet further appreciated that a function of VGAM1361 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGAM1361 correlate with, and may be deduced from, the identity of the host target genes which VGAM1361 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47930] Nucleotide sequences of the VGAM1361 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1361 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1361 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1361 are further

described hereinbelow with reference to Table 1.

[47931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1361 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1361 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47932] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1361 gene, herein designated VGAM is inhibition of expression of VGAM1361 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1361 correlate with, and may be deduced from, the identity of the target genes which VGAM1361 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47933] BUB3 Budding Uninhibited By Benzimidazoles 3 Homolog (yeast) (BUB3, Accession NM_004725) is a VGAM1361 host target gene. BUB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BUB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of BUB3 BINDING SITE, designated SEQ ID:11096, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47934] A function of VGAM1361 is therefore inhibition of BUB3 Budding Uninhibited By Benzimidazoles 3 Homolog (yeast) (BUB3, Accession NM_004725), a gene which has a role in the mitotic spindle checkpoint. Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BUB3. The function of BUB3 has been established by previous studies. A feedback control mechanism, or cell cycle checkpoint, delays the onset of anaphase until all the chromosomes are correctly aligned on the mitotic spindle. Mutations in the *S. cerevisiae* BUB and MAD genes abolish this checkpoint, such that mutant cells fail to undergo mitotic arrest in response to spindle damage. The yeast BUB1 (see OMIM Ref. No. 602452) gene encodes a protein kinase that can bind and phosphorylate BUB3. Mammalian BUB1 localizes to the kinetochore of unaligned chromosomes. To further characterize the role of BUB1 in mitosis, Taylor et al. (1998) searched an EST database to identify the human homolog of BUB3. They identified a partial hu-

man BUB3 cDNA and used a PCR strategy to isolate a full-length cDNA. The predicted 328-amino acid human protein shares approximately 34% identity with yeast BUB3. Both proteins contain 4 WD repeats. When expressed in mammalian cells, a chimeric GFP-BUB3 protein localized to kinetochores before chromosome alignment. Using deletion analysis, the authors identified a domain of BUB1 that is required both for binding BUB3 and for kinetochore localization of BUB1. Taylor et al. (1998) reported that a similar domain in BUBR1 (OMIM Ref. No. 602860) mediates binding to BUB3. They suggested that the BUB and MAD proteins may be part of a large protein complex that is recruited to unattached kinetochores and that dissociates from kinetochores upon achieving correct bipolar attachment. Animal model experiments lend further support to the function of BUB3. By gene-targeting techniques, Kalitsis et al. (2000) disrupted the Bub3 gene in mice, which resulted in embryonic lethality prior to day 8.5 postcoitum (pc) in homozygous mutants. Mutant embryos appeared normal at day 3.5 pc but rapidly degenerated. An observed accumulation of mitotic errors suggested that Bub3 is essential for normal mitosis and for early embryonic development in the mouse.

[47935] It is appreciated that the abovementioned animal model for BUB3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[47936] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[47937] Kalitsis, P.; Earle, E.; Fowler, K. J.; Choo, K. H. A. : Bub3 gene disruption in mice reveals essential mitotic spindle checkpoint function during early embryogenesis. *Genes Dev.* 14: 2277–2282, 2000. ; and

[47938] Taylor, S. S.; Ha, E.; McKeon, F. : The human homologue of Bub3 is required for kinetochore localization of Bub1 and a Mad3/Bub1–related protein kinase. *J. Cell Biol.* 142: 1–11, 1998.

[47939] Further studies establishing the function and utilities of BUB3 are found in John Hopkins OMIM database record ID 603719, and in cited publications numbered 275 and 5362 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear RNA Export Factor 2 (NXF2, Accession NM_017809) is another VGAM1361 host target gene. NXF2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region

of mRNA encoded by NXF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXF2 BINDING SITE, designated SEQ ID:19457, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47940] Another function of VGAM1361 is therefore inhibition of Nuclear RNA Export Factor 2 (NXF2, Accession NM_017809), a gene which is involved in the export of mrna from the nucleus to the cytoplasm. Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXF2. The function of NXF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 5 (RPS6KA5, Accession NM_004755) is another VGAM1361 host target gene. RPS6KA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of RPS6KA5 BINDING SITE, designated SEQ ID:11141, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47941] Another function of VGAM1361 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 5 (RPS6KA5, Accession NM_004755), a gene which plays an essential role in the proliferation of yeast cells. Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA5. The function of RPS6KA5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM191. Zinc Finger Protein 2 (A1-5) (ZNF2, Accession NM_021088) is another VGAM1361 host target gene. ZNF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF2 BINDING SITE, designated SEQ ID:22066, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4072.

[47942] Another function of VGAM1361 is therefore inhibition of Zinc Finger Protein 2 (A1-5) (ZNF2, Accession NM_021088). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF2. FLJ11004 (Accession NM_018296) is another VGAM1361 host target gene. FLJ11004 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11004 BINDING SITE, designated SEQ ID:20287, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47943] Another function of VGAM1361 is therefore inhibition of FLJ11004 (Accession NM_018296). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11004. MOST2 (Accession NM_020250) is another VGAM1361 host target gene. MOST2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MOST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOST2 BINDING SITE, designated SEQ ID:21555, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47944] Another function of VGAM1361 is therefore inhibition of MOST2 (Accession NM_020250). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOST2. Ras Protein-specific Guanine Nucleotide-releasing Factor 2 (RASGRF2, Accession XM_027943) is another VGAM1361 host target gene. RASGRF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASGRF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASGRF2 BINDING SITE, designated SEQ ID:30596, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47945] Another function of VGAM1361 is therefore inhibition of

Ras Protein-specific Guanine Nucleotide-releasing Factor 2 (RASGRF2, Accession XM_027943). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRF2. LOC219688 (Accession XM_167568) is another VGAM1361 host target gene. LOC219688 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219688 BINDING SITE, designated SEQ ID:44696, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47946] Another function of VGAM1361 is therefore inhibition of LOC219688 (Accession XM_167568). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219688. LOC221663 (Accession XM_168131) is another VGAM1361 host target gene. LOC221663 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221663, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221663 BINDING SITE, designated SEQ ID:45037, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47947] Another function of VGAM1361 is therefore inhibition of LOC221663 (Accession XM_168131). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221663. LOC51336 (Accession NM_016646) is another VGAM1361 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51336 BINDING SITE, designated SEQ ID:18752, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47948] Another function of VGAM1361 is therefore inhibition of LOC51336 (Accession NM_016646). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC51336. LOC90670 (Accession XM_033352) is another VGAM1361 host target gene. LOC90670 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90670, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90670 BINDING SITE, designated SEQ ID:31885, to the nucleotide sequence of VGAM1361 RNA, herein designated VGAM RNA, also designated SEQ ID:4072.

[47949] Another function of VGAM1361 is therefore inhibition of LOC90670 (Accession XM_033352). Accordingly, utilities of VGAM1361 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90670. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1362 (VGAM1362) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47950] VGAM1362 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1362 was detected is described hereinabove with reference to Figs. 1–8.

[47951] VGAM1362 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck Adenovirus 1.

VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47952] VGAM1362 gene encodes a VGAM1362 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1362 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1362 precursor RNA is designated SEQ ID:1348, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1348 is located at position 12491 relative to the genome of Duck Adenovirus 1.

[47953] VGAM1362 precursor RNA folds onto itself, forming VGAM1362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47954] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1362 folded precursor RNA into VGAM1362 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1362 RNA is designated SEQ ID:4073, and is provided hereinbelow with reference to the sequence listing part.

[47955] VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1362 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47956] VGAM1362 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1362 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1362 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[47957] The complementary binding of VGAM1362 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1362 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1362 host target RNA into VGAM1362 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47958] It is appreciated that VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1362 host target genes. The mRNA of each one of this plurality of VGAM1362 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1362 RNA, herein designated VGAM RNA, and which when bound by VGAM1362 RNA causes inhibition of translation of respective one or more VGAM1362 host target proteins.

[47959] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1362 gene, herein designated VGAM GENE, on one or more VGAM1362 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[47960] It is yet further appreciated that a function of VGAM1362 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGAM1362 correlate with, and may be deduced from, the identity of the host target genes which VGAM1362 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47961] Nucleotide sequences of the VGAM1362 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1362 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1362 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1362 are further described hereinbelow with reference to Table 1.

[47962] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1362 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1362 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47963] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1362 gene, herein designated VGAM is inhibition of expression of VGAM1362 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1362 correlate with, and may be deduced from, the identity of the target genes which VGAM1362 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47964] BS69 (Accession NM_006624) is a VGAM1362 host target gene. BS69 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BS69, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BS69 BINDING SITE, designated SEQ ID:13406, to the nucleotide sequence of VGAM1362 RNA, herein designated VGAM RNA, also designated SEQ ID:4073.

[47965] A function of VGAM1362 is therefore inhibition of BS69 (Accession NM_006624). Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BS69. FLJ23590 (Accession NM_024649) is another VGAM1362 host target gene. FLJ23590 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23590, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23590 BINDING SITE, designated SEQ ID:23939, to the nucleotide sequence of VGAM1362 RNA, herein designated VGAM RNA, also designated SEQ ID:4073.

[47966] Another function of VGAM1362 is therefore inhibition of FLJ23590 (Accession NM_024649). Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ23590. KIAA0993 (Accession XM_034413) is another VGAM1362 host target gene. KIAA0993 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0993 BINDING SITE, designated SEQ ID:32075, to the nucleotide sequence of VGAM1362 RNA, herein designated VGAM RNA, also designated SEQ ID:4073.

[47967] Another function of VGAM1362 is therefore inhibition of KIAA0993 (Accession XM_034413). Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0993. LOC222001 (Accession XM_167489) is another VGAM1362 host target gene. LOC222001 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222001 BINDING SITE, designated SEQ ID:44642, to the nucleotide sequence of VGAM1362 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4073.

[47968] Another function of VGAM1362 is therefore inhibition of LOC222001 (Accession XM_167489). Accordingly, utilities of VGAM1362 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222001. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1363 (VGAM1363) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47969] VGAM1363 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1363 was detected is described hereinabove with reference to Figs. 1–8.

[47970] VGAM1363 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck Adenovirus 1. VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47971] VGAM1363 gene encodes a VGAM1363 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1363 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1363 precursor RNA is designated SEQ ID:1349, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1349 is located at position 14923 relative to the genome of Duck Adenovirus 1.

[47972] VGAM1363 precursor RNA folds onto itself, forming VGAM1363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[47973] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1363 folded precursor RNA into VGAM1363 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1363 RNA is designated SEQ ID:4074, and is provided hereinbelow with reference to the sequence listing part.

[47974] VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1363 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[47975] VGAM1363 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1363 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1363 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[47976] The complementary binding of VGAM1363 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1363 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1363 host target RNA into VGAM1363 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[47977] It is appreciated that VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1363 host target genes. The mRNA of

each one of this plurality of VGAM1363 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1363 RNA, herein designated VGAM RNA, and which when bound by VGAM1363 RNA causes inhibition of translation of respective one or more VGAM1363 host target proteins.

[47978] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1363 gene, herein designated VGAM GENE, on one or more VGAM1363 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[47979] It is yet further appreciated that a function of VGAM1363 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGAM1363 correlate with, and may be deduced from, the identity of the host target genes which VGAM1363 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[47980] Nucleotide sequences of the VGAM1363 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1363 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1363 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1363 are further described hereinbelow with reference to Table 1.

[47981] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1363 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1363 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[47982] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1363 gene, herein designated VGAM is inhibition of expression of VGAM1363 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1363 correlate with, and may be deduced from, the identity of the target genes which VGAM1363 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[47983] Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202) is a VGAM1363 host target gene. TCF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF7 BINDING SITE, designated SEQ ID:9193, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47984] A function of VGAM1363 is therefore inhibition of Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202). Accordingly, utilities of VGAM1363

include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF7. Ras Homolog Gene Family, Member U (ARHU, Accession NM_021205) is another VGAM1363 host target gene. ARHU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHU BINDING SITE, designated SEQ ID:22179, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47985] Another function of VGAM1363 is therefore inhibition of Ras Homolog Gene Family, Member U (ARHU, Accession NM_021205). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHU. KIAA0194 (Accession XM_038362) is another VGAM1363 host target gene. KIAA0194 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KIAA0194 BINDING SITE, designated SEQ ID:32826, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47986] Another function of VGAM1363 is therefore inhibition of KIAA0194 (Accession XM_038362). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0194. KIAA0222 (Accession NM_014643) is another VGAM1363 host target gene. KIAA0222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0222 BINDING SITE, designated SEQ ID:16044, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47987] Another function of VGAM1363 is therefore inhibition of KIAA0222 (Accession NM_014643). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0222. Progesterone Receptor Membrane Component

2 (PGRMC2, Accession NM_006320) is another VGAM1363 host target gene. PGRMC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PGRMC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGRMC2 BINDING SITE, designated SEQ ID:13011, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47988] Another function of VGAM1363 is therefore inhibition of Progesterone Receptor Membrane Component 2 (PGRMC2, Accession NM_006320). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGRMC2. SAM Domain and HD Domain 1 (SAMHD1, Accession XM_028704) is another VGAM1363 host target gene. SAMHD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SAMHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAMHD1 BINDING SITE, designated SEQ

ID:30734, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47989] Another function of VGAM1363 is therefore inhibition of SAM Domain and HD Domain 1 (SAMHD1, Accession XM_028704). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAMHD1. TSPEAR (Accession NM_144991) is another VGAM1363 host target gene. TSPEAR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSPEAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSPEAR BINDING SITE, designated SEQ ID:29596, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47990] Another function of VGAM1363 is therefore inhibition of TSPEAR (Accession NM_144991). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSPEAR. LOC148529 (Accession XM_097481) is another

VGAM1363 host target gene. LOC148529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148529 BINDING SITE, designated SEQ ID:40890, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47991] Another function of VGAM1363 is therefore inhibition of LOC148529 (Accession XM_097481). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148529. LOC148823 (Accession NM_145278) is another VGAM1363 host target gene. LOC148823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148823 BINDING SITE, designated SEQ ID:29792, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47992] Another function of VGAM1363 is therefore inhibition of LOC148823 (Accession NM_145278). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148823. LOC220963 (Accession XM_166145) is another VGAM1363 host target gene. LOC220963 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220963, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220963 BINDING SITE, designated SEQ ID:43955, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47993] Another function of VGAM1363 is therefore inhibition of LOC220963 (Accession XM_166145). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220963. LOC221337 (Accession XM_166387) is another VGAM1363 host target gene. LOC221337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221337, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221337 BINDING SITE, designated SEQ ID:44234, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47994] Another function of VGAM1363 is therefore inhibition of LOC221337 (Accession XM_166387). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221337. LOC255671 (Accession XM_173196) is another VGAM1363 host target gene. LOC255671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255671 BINDING SITE, designated SEQ ID:46438, to the nucleotide sequence of VGAM1363 RNA, herein designated VGAM RNA, also designated SEQ ID:4074.

[47995] Another function of VGAM1363 is therefore inhibition of LOC255671 (Accession XM_173196). Accordingly, utilities of VGAM1363 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255671. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1364 (VGAM1364) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[47996] VGAM1364 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1364 was detected is described hereinabove with reference to Figs. 1–8.

[47997] VGAM1364 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck Adenovirus 1. VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[47998] VGAM1364 gene encodes a VGAM1364 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1364 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1364 precursor RNA is designated SEQ ID:1350, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1350 is located at position 14767 relative to the genome of Duck Adenovirus 1.

- [47999] VGAM1364 precursor RNA folds onto itself, forming VGAM1364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48000] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1364 folded precursor RNA into VGAM1364 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1364 RNA is designated SEQ ID:4075, and is provided hereinbelow with reference to the sequence listing part.

[48001] VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1364 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48002] VGAM1364 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1364 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1364 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48003] The complementary binding of VGAM1364 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1364 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1364 host target RNA into VGAM1364 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48004] It is appreciated that VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1364 host target genes. The mRNA of each one of this plurality of VGAM1364 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1364 RNA, herein designated VGAM RNA, and which when bound by VGAM1364 RNA causes

inhibition of translation of respective one or more VGAM1364 host target proteins.

[48005] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1364 gene, herein designated VGAM GENE, on one or more VGAM1364 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48006] It is yet further appreciated that a function of VGAM1364 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1364 include diagnosis, prevention and

treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGAM1364 correlate with, and may be deduced from, the identity of the host target genes which VGAM1364 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48007] Nucleotide sequences of the VGAM1364 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1364 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1364 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1364 are further described hereinbelow with reference to Table 1.

[48008] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1364 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1364 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48009] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1364 gene, herein designated VGAM is inhibition of expression of VGAM1364 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1364 correlate with, and may be deduced from, the identity of the target genes which VGAM1364 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48010] Solute Carrier Family 25 (mitochondrial carrier; ornithine transporter) Member 15 (SLC25A15, Accession NM_014252) is a VGAM1364 host target gene. SLC25A15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC25A15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC25A15 BINDING SITE, designated SEQ ID:15526, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48011] A function of VGAM1364 is therefore inhibition of Solute Carrier Family 25 (mitochondrial carrier; ornithine transporter) Member 15 (SLC25A15, Accession NM_014252), a gene which participates the ornithine transport across inner mitochondrial membrane, from the cytoplasm to the matrix. Accordingly, utilities of VGAM1364 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with SLC25A15. The function of SLC25A15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM_005432) is another VGAM1364 host target gene. XRCC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC3 BINDING SITE, designated SEQ ID:11906, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48012] Another function of VGAM1364 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 3 (XRCC3, Accession NM_005432), a gene which is required for meiotic recombination, synaptonemal complex formation and cell cycle progression. Accordingly, utilities of VGAM1364 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with XRCC3. The function of XRCC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1290.FLJ00060 (Accession XM_028154) is another VGAM1364 host target gene.

FLJ00060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ00060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00060 BINDING SITE, designated SEQ ID:30627, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48013] Another function of VGAM1364 is therefore inhibition of FLJ00060 (Accession XM_028154). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00060. FLJ12969 (Accession NM_022838) is another VGAM1364 host target gene. FLJ12969 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12969, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12969 BINDING SITE, designated SEQ ID:23124, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48014] Another function of VGAM1364 is therefore inhibition of FLJ12969 (Accession NM_022838). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12969. FLJ13189 (Accession NM_024882) is another VGAM1364 host target gene. FLJ13189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13189 BINDING SITE, designated SEQ ID:24328, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48015] Another function of VGAM1364 is therefore inhibition of FLJ13189 (Accession NM_024882). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13189. Forkhead Box P1 (FOXP1, Accession NM_032682) is another VGAM1364 host target gene. FOXP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FOXP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXP1 BINDING SITE, designated SEQ ID:26403, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48016] Another function of VGAM1364 is therefore inhibition of Forkhead Box P1 (FOXP1, Accession NM_032682). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXP1. Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM_015084) is another VGAM1364 host target gene. MRPS27 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MRPS27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MRPS27 BINDING SITE, designated SEQ ID:17471, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48017] Another function of VGAM1364 is therefore inhibition of Mitochondrial Ribosomal Protein S27 (MRPS27, Accession NM_015084). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS27. LOC157773 (Accession XM_088387) is another VGAM1364 host target gene. LOC157773 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157773 BINDING SITE, designated SEQ ID:39669, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48018] Another function of VGAM1364 is therefore inhibition of LOC157773 (Accession XM_088387). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157773. LOC162333 (Accession XM_102591) is another VGAM1364 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42122, to the nucleotide sequence of VGAM1364 RNA, herein designated VGAM RNA, also designated SEQ ID:4075.

[48019] Another function of VGAM1364 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1364 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1365 (VGAM1365) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48020] VGAM1365 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1365 was detected is described hereinabove with reference to Figs. 1–8.

[48021] VGAM1365 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Duck Adenovirus 1.

VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48022] VGAM1365 gene encodes a VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1365 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1365 precursor RNA is designated SEQ ID:1351, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1351 is located at position 10633 relative to the genome of Duck Adenovirus 1.

[48023] VGAM1365 precursor RNA folds onto itself, forming VGAM1365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48024] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1365 folded precursor RNA into VGAM1365 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 93%) nucleotide sequence of VGAM1365 RNA is designated SEQ ID:4076, and is provided hereinbelow with reference to the sequence listing part.

[48025] VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1365 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48026] VGAM1365 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1365 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1365 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48027] The complementary binding of VGAM1365 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1365 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1365 host target RNA into VGAM1365 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48028] It is appreciated that VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1365 host target genes. The mRNA of each one of this plurality of VGAM1365 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1365 RNA, herein designated VGAM RNA, and which when bound by VGAM1365 RNA causes inhibition of translation of respective one or more VGAM1365 host target proteins.

[48029] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1365 gene, herein designated VGAM GENE, on one or more VGAM1365 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48030] It is yet further appreciated that a function of VGAM1365 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGAM1365 correlate with, and may be deduced from, the identity of the host target genes which VGAM1365 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48031] Nucleotide sequences of the VGAM1365 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1365 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1365 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1365 are further described hereinbelow with reference to Table 1.

[48032] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1365 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1365 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48033] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1365 gene, herein designated VGAM is inhibition of expression of VGAM1365 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1365 correlate with, and may be deduced from, the identity of the target genes which VGAM1365 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48034] Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398) is a VGAM1365 host target gene. DLG5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DLG5, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG5 BINDING SITE, designated SEQ ID:40334, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48035] A function of VGAM1365 is therefore inhibition of Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398), a gene which may transmit extracellular signals to inhibit cell proliferation. Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG5. The function of DLG5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444. Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242) is another VGAM1365 host target gene. MBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBL2 BIND-

ING SITE, designated SEQ ID:5760, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48036] Another function of VGAM1365 is therefore inhibition of Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBL2. DKFZp566H0824 (Accession NM_017535) is another VGAM1365 host target gene. DKFZp566H0824 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp566H0824, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566H0824 BINDING SITE, designated SEQ ID:18975, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48037] Another function of VGAM1365 is therefore inhibition of DKFZp566H0824 (Accession NM_017535). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp566H0824. DKFZP566J091 (Accession NM_030915) is another VGAM1365 host target gene. DKFZP566J091 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP566J091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566J091 BINDING SITE, designated SEQ ID:25185, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48038] Another function of VGAM1365 is therefore inhibition of DKFZP566J091 (Accession NM_030915). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566J091. FLJ10901 (Accession NM_018265) is another VGAM1365 host target gene. FLJ10901 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10901 BINDING SITE, designated SEQ ID:20228, to the

nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48039] Another function of VGAM1365 is therefore inhibition of FLJ10901 (Accession NM_018265). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10901. GW112 (Accession NM_006418) is another VGAM1365 host target gene. GW112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GW112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GW112 BINDING SITE, designated SEQ ID:13132, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48040] Another function of VGAM1365 is therefore inhibition of GW112 (Accession NM_006418). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GW112. KIAA0993 (Accession XM_034413) is another VGAM1365 host target gene. KIAA0993 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by KIAA0993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0993 BINDING SITE, designated SEQ ID:32080, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48041] Another function of VGAM1365 is therefore inhibition of KIAA0993 (Accession XM_034413). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0993. KIAA1822 (Accession XM_041566) is another VGAM1365 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33550, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48042] Another function of VGAM1365 is therefore inhibition of KIAA1822 (Accession XM_041566). Accordingly, utilities

of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168) is another VGAM1365 host target gene. PAK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK6 BINDING SITE, designated SEQ ID:21388, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48043] Another function of VGAM1365 is therefore inhibition of p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK6. Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession NM_014452) is another VGAM1365 host target gene. TNFRSF21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF21 BINDING SITE, designated SEQ ID:15802, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48044] Another function of VGAM1365 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 21 (TNFRSF21, Accession NM_014452). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF21. LOC120892 (Accession XM_058513) is another VGAM1365 host target gene. LOC120892 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120892, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120892 BINDING SITE, designated SEQ ID:36648, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48045] Another function of VGAM1365 is therefore inhibition of LOC120892 (Accession XM_058513). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC120892. LOC157653 (Accession XM_088353) is another VGAM1365 host target gene. LOC157653 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157653, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157653 BINDING SITE, designated SEQ ID:39633, to the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48046] Another function of VGAM1365 is therefore inhibition of LOC157653 (Accession XM_088353). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157653. LOC245771 (Accession XM_167366) is another VGAM1365 host target gene. LOC245771 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC245771, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245771 BINDING SITE, designated SEQ ID:44633, to

the nucleotide sequence of VGAM1365 RNA, herein designated VGAM RNA, also designated SEQ ID:4076.

[48047] Another function of VGAM1365 is therefore inhibition of LOC245771 (Accession XM_167366). Accordingly, utilities of VGAM1365 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245771. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1366 (VGAM1366) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48048] VGAM1366 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1366 was detected is described hereinabove with reference to Figs. 1–8.

[48049] VGAM1366 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48050] VGAM1366 gene encodes a VGAM1366 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1366 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1366 precursor RNA is designated SEQ ID:1352, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1352 is located at position 50024 relative to the genome of Human Herpesvirus 6.

[48051] VGAM1366 precursor RNA folds onto itself, forming VGAM1366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48052] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1366 folded precursor RNA into VGAM1366 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1366 RNA is designated SEQ ID:4077, and is provided hereinbelow with reference to the sequence listing part.

[48053] VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1366 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48054] VGAM1366 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1366 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1366 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48055] The complementary binding of VGAM1366 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1366 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1366 host target RNA into VGAM1366 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48056] It is appreciated that VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1366 host target genes. The mRNA of each one of this plurality of VGAM1366 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1366 RNA, herein designated VGAM RNA, and which when bound by VGAM1366 RNA causes inhibition of translation of respective one or more VGAM1366 host target proteins.

[48057] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1366 gene, herein designated VGAM GENE, on one or more VGAM1366 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[48058] It is yet further appreciated that a function of VGAM1366 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1366 correlate with, and may be deduced from, the identity of the host target genes which VGAM1366 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48059] Nucleotide sequences of the VGAM1366 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1366 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1366 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1366 are further described hereinbelow with reference to Table 1.

[48060] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1366 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1366 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48061] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1366 gene, herein designated VGAM is inhibition of expression of VGAM1366 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1366 correlate with, and may be deduced from, the identity of the target genes which VGAM1366 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48062] V-erb-b2 Erythroblastic Leukemia Viral Oncogene Homolog 2, Neuro/glioblastoma Derived Oncogene Homolog (avian) (ERBB2, Accession NM_004448) is a VGAM1366 host target gene. ERBB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERBB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERBB2 BINDING SITE, designated SEQ ID:10745, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48063] A function of VGAM1366 is therefore inhibition of V-erb-b2 Erythroblastic Leukemia Viral Oncogene Homolog 2, Neuro/glioblastoma Derived Oncogene Homolog (avian) (ERBB2, Accession NM_004448), a gene which Tyrosine kinase receptor. Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERBB2. The function of ERBB2 has been established by previous studies. The oncogene originally called NEU was derived from rat neuro/glioblastoma cell lines. It encodes a tumor antigen, p185, which is serologically related to EGFR, the epidermal growth factor receptor (OMIM Ref. No. 131550). EGFR maps to chromosome 7. Yang-Feng et al. (1985) found, however, that the human homolog, which they designated NGL (to avoid confusion with neuraminidase, which is also symbolized NEU), maps to 17q12-q22 by in situ hybridization and to 17q21-qter in somatic cell hybrids. Thus, the SRO is 17q21-q22. Coussens et al. (1985) identified a potential cell surface receptor of the tyrosine kinase gene family and characterized it by cloning the gene. Its primary sequence is very similar to that of the human epidermal growth factor receptor. Because of the seemingly close relationship to the human EGF receptor, the

authors called the gene HER2. By Southern blot analysis of somatic cell hybrid DNA and by in situ hybridization, the gene was assigned to 17q21–q22. This chromosomal location of the gene is coincident with the NEU oncogene, which suggests that the 2 genes may in fact be the same; indeed, sequencing indicates that they are identical (Francke, 1988). Van de Vijver et al. (1988) found a correlation between overexpression of NEU protein and the large-cell, comedo growth type of ductal carcinoma. They could find no correlation, however, with lymph-node status or tumor recurrence. Slamon et al. (1989) described the role of HER2/NEU in breast (OMIM Ref. No. 114480) and ovarian cancer (OMIM Ref. No. 167000), which together account for one-third of all cancers in women and approximately one-quarter of cancer-related deaths in females. The HER2 gene is amplified and HER2 is overexpressed in 25 to 30% of breast cancers, increasing the aggressiveness of the tumor. Slamon et al. (2001) found that herceptin increased the clinical benefit of first-line chemotherapy in metastatic breast cancer that overexpresses HER2. In a population-based case control study of the val655-to-ile polymorphism (164870.0001), Xie et al. (2000) found that the val allele was associated with an in-

creased risk of breast cancer, particularly among younger women. Because of the significant ethnic differences in the incidence of breast cancer and other solid tumors, Ameyaw et al. (2002) undertook a study of 7 ethnic groups from 3 separate continents. The frequency of the val allele was highly variable between populations (1 to 24%). The continental African populations had a lower frequency than did the other subjects, corresponding with the lower incidence and lower risk of breast cancer in African women compared with Caucasian and African-American women. Animal model experiments lend further support to the function of ERBB2. An activated mutant form of ERBB2 is rarely found in human cancer. Instead, wildtype ERBB2 is overexpressed and/or amplified in 10 to 30% of breast cancers, where it correlates with chemoresistance and poor patient prognosis. Herceptin, a monoclonal antibody against ERBB2, is an effective treatment for a subset of patients with advanced breast cancer. Liu et al. (2002) used a transgenic mouse model with targeted aberrant overexpression of ERBB2 to determine whether genetic instability is associated with mammary tumorigenesis in vivo in the absence of heritable defects in known DNA maintenance genes.

[48064] It is appreciated that the abovementioned animal model for ERBB2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[48065] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48066] Coussens, L.; Yang-Feng, T. L.; Liao, Y.-C.; Chen, E.; Gray, A.; McGrath, J.; Seeburg, P. H.; Libermann, T. A.; Schlessinger, J.; Francke, U.; Levinson, A.; Ullrich, A. : Tyrosine kinase receptor with extensive homology to EGF receptor shares chromosomal location with NEU oncogene. Science 230: 1132-1139, 1985. ; and

[48067] Liu, S.; Liu, W.; Jakubczak, J. L.; Erexson, G. L.; Tindall, K. R.; Chan, R.; Muller, W. J.; Adhya, S.; Garges, S.; Merlino, G. : Genetic instability favoring transversions associated w.

[48068] Further studies establishing the function and utilities of ERBB2 are found in John Hopkins OMIM database record ID 164870, and in sited publications numbered 1826-1827, 11591-2086, 11999-2102, 274 and 3136-3140 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.Forkhead

Box D2 (FOXD2, Accession NM_004474) is another VGAM1366 host target gene. FOXD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FOXD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXD2 BINDING SITE, designated SEQ ID:10787, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48069] Another function of VGAM1366 is therefore inhibition of Forkhead Box D2 (FOXD2, Accession NM_004474). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXD2. Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM_166287) is another VGAM1366 host target gene. ACAA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ACAA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAA2 BINDING SITE, des-

ignated SEQ ID:44096, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48070] Another function of VGAM1366 is therefore inhibition of Acetyl-Coenzyme A Acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (ACAA2, Accession XM_166287). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAA2. Conserved Helix-loop-helix Ubiquitous Kinase (CHUK, Accession NM_001278) is another VGAM1366 host target gene. CHUK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHUK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHUK BINDING SITE, designated SEQ ID:6947, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48071] Another function of VGAM1366 is therefore inhibition of Conserved Helix-loop-helix Ubiquitous Kinase (CHUK, Accession NM_001278). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with CHUK. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380) is another VGAM1366 host target gene. DDX28 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DDX28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX28 BINDING SITE, designated SEQ ID:20409, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48072] Another function of VGAM1366 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX28. DIS3 (Accession NM_014953) is another VGAM1366 host target gene. DIS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of DIS3 BINDING SITE, designated SEQ ID:17303, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48073] Another function of VGAM1366 is therefore inhibition of DIS3 (Accession NM_014953). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIS3. DJ328E19.C1.1 (Accession NM_015383) is another VGAM1366 host target gene. DJ328E19.C1.1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DJ328E19.C1.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ328E19.C1.1 BINDING SITE, designated SEQ ID:17683, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48074] Another function of VGAM1366 is therefore inhibition of DJ328E19.C1.1 (Accession NM_015383). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ328E19.C1.1. FLJ21032 (Accession NM_024906) is

another VGAM1366 host target gene. FLJ21032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21032 BINDING SITE, designated SEQ ID:24398, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48075] Another function of VGAM1366 is therefore inhibition of FLJ21032 (Accession NM_024906). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21032. FLJ21817 (Accession NM_022448) is another VGAM1366 host target gene. FLJ21817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21817 BINDING SITE, designated SEQ ID:22783, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48076] Another function of VGAM1366 is therefore inhibition of FLJ21817 (Accession NM_022448). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21817. G-protein Coupled Receptor 88 (GPR88, Accession NM_022049) is another VGAM1366 host target gene. GPR88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR88 BINDING SITE, designated SEQ ID:22573, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48077] Another function of VGAM1366 is therefore inhibition of G-protein Coupled Receptor 88 (GPR88, Accession NM_022049). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR88. G Protein Pathway Suppressor 2 (GPS2, Accession NM_004489) is another VGAM1366 host target gene. GPS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by GPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPS2 BINDING SITE, designated SEQ ID:10825, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48078] Another function of VGAM1366 is therefore inhibition of G Protein Pathway Suppressor 2 (GPS2, Accession NM_004489). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPS2. KIAA0295 (Accession XM_042833) is another VGAM1366 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33786, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48079] Another function of VGAM1366 is therefore inhibition of

KIAA0295 (Accession XM_042833). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. KIAA0561 (Accession XM_038150) is another VGAM1366 host target gene. KIAA0561 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0561, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0561 BINDING SITE, designated SEQ ID:32766, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48080] Another function of VGAM1366 is therefore inhibition of KIAA0561 (Accession XM_038150). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0561. KIAA1826 (Accession XM_040784) is another VGAM1366 host target gene. KIAA1826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1826 BINDING SITE, designated SEQ ID:33378, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48081] Another function of VGAM1366 is therefore inhibition of KIAA1826 (Accession XM_040784). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1826. MGC3184 (Accession NM_030965) is another VGAM1366 host target gene. MGC3184 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3184 BINDING SITE, designated SEQ ID:25232, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48082] Another function of VGAM1366 is therefore inhibition of MGC3184 (Accession NM_030965). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3184. MGC5139 (Accession XM_058587) is another

VGAM1366 host target gene. MGC5139 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC5139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5139 BINDING SITE, designated SEQ ID:36679, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48083] Another function of VGAM1366 is therefore inhibition of MGC5139 (Accession XM_058587). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5139. Neurexophilin 3 (NXPH3, Accession XM_037847) is another VGAM1366 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32720, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ

ID:4077.

[48084] Another function of VGAM1366 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM_037847). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. P11 (Accession NM_006025) is another VGAM1366 host target gene. P11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P11 BINDING SITE, designated SEQ ID:12642, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48085] Another function of VGAM1366 is therefore inhibition of P11 (Accession NM_006025). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P11. LOC127262 (Accession XM_072073) is another VGAM1366 host target gene. LOC127262 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127262, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127262 BINDING SITE, designated SEQ ID:37459, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48086] Another function of VGAM1366 is therefore inhibition of LOC127262 (Accession XM_072073). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127262. LOC149013 (Accession XM_086398) is another VGAM1366 host target gene. LOC149013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149013 BINDING SITE, designated SEQ ID:38633, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48087] Another function of VGAM1366 is therefore inhibition of LOC149013 (Accession XM_086398). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149013. LOC149317 (Accession XM_086493) is another VGAM1366 host target gene. LOC149317 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149317 BINDING SITE, designated SEQ ID:38709, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48088] Another function of VGAM1366 is therefore inhibition of LOC149317 (Accession XM_086493). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149317. LOC220638 (Accession XM_058247) is another VGAM1366 host target gene. LOC220638 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220638, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220638 BINDING SITE, designated SEQ ID:36589, to

the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48089] Another function of VGAM1366 is therefore inhibition of LOC220638 (Accession XM_058247). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220638. LOC221975 (Accession XM_166534) is another VGAM1366 host target gene. LOC221975 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221975 BINDING SITE, designated SEQ ID:44496, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48090] Another function of VGAM1366 is therefore inhibition of LOC221975 (Accession XM_166534). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221975. LOC257031 (Accession XM_170583) is another VGAM1366 host target gene. LOC257031 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257031 BINDING SITE, designated SEQ ID:45390, to the nucleotide sequence of VGAM1366 RNA, herein designated VGAM RNA, also designated SEQ ID:4077.

[48091] Another function of VGAM1366 is therefore inhibition of LOC257031 (Accession XM_170583). Accordingly, utilities of VGAM1366 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257031. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1367 (VGAM1367) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48092] VGAM1367 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1367 was detected is described hereinabove with reference to Figs. 1-8.

[48093] VGAM1367 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human Herpesvirus 6. VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48094] VGAM1367 gene encodes a VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1367 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1367 precursor RNA is designated SEQ ID:1353, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1353 is located at position 48800 relative to the genome of Human Herpesvirus 6.

[48095] VGAM1367 precursor RNA folds onto itself, forming VGAM1367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1367 folded precursor RNA into VGAM1367 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1367 RNA is designated SEQ ID:4078, and is provided hereinbelow with reference to the sequence listing part.

[48097] VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1367 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48098] VGAM1367 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1367 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1367 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48099] The complementary binding of VGAM1367 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1367 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1367

host target RNA into VGAM1367 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48100] It is appreciated that VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1367 host target genes. The mRNA of each one of this plurality of VGAM1367 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1367 RNA, herein designated VGAM RNA, and which when bound by VGAM1367 RNA causes inhibition of translation of respective one or more VGAM1367 host target proteins.

[48101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1367 gene, herein designated VGAM GENE, on one or more VGAM1367 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48102] It is yet further appreciated that a function of VGAM1367 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1367 correlate with, and may be deduced from, the identity of the host target genes which VGAM1367 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48103] Nucleotide sequences of the VGAM1367 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1367 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1367 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1367 are further

described hereinbelow with reference to Table 1.

[48104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1367 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1367 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1367 gene, herein designated VGAM is inhibition of expression of VGAM1367 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1367 correlate with, and may be deduced from, the identity of the target genes which VGAM1367 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48106] Branched Chain Aminotransferase 1, Cytosolic (BCAT1, Accession XM_038659) is a VGAM1367 host target gene. BCAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of BCAT1 BINDING SITE, designated SEQ ID:32896, to the nucleotide sequence of VGAM1367 RNA, herein designated VGAM RNA, also designated SEQ ID:4078.

[48107] A function of VGAM1367 is therefore inhibition of Branched Chain Aminotransferase 1, Cytosolic (BCAT1, Accession XM_038659), a gene which catalyzes of the essential branched chain leucine, isoleucine, and valine. Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCAT1. The function of BCAT1 has been established by previous studies. Jones and Moore (1976) isolated an auxotrophic mutant in Chinese-hamster ovary cells that lacks the ability to grow if alpha-ketoisovaleric acid, alpha-ketoisocaproic acid and alpha-keto-beta-methylvaleric acid are substituted for valine, leucine and isoleucine in the culture medium. This auxotroph, called TRANS-minus, is caused by lack of the enzyme branched-chain amino acid transaminase (BCT). Jones and Moore (1979) provisionally assigned the BCT1 gene to 12pter-q12. Naylor and Shows (1979, 1980) also assigned BCT1 to chromosome 12 and BCT2 (OMIM Ref. No. 113530) to chromosome 19. There may be 2 different

clinical disorders due to defect of branched-chain amino acid transamination, hypervalinemia (OMIM Ref. No. 277100) and hyperleucine-isoleucinemia (OMIM Ref. No. 238340). Since there are 2 distinct BCATs (see OMIM Ref. No. 113530), it is possible that one is mutant in each of these 2 conditions. Animal model experiments lend further support to the function of BCAT1. In the mouse, Benvenisty et al. (1992) isolated the Bcat1 gene by a subtraction/coexpression strategy with Myc-induced tumors of transgenic mice, and proved that Bcat1 is a direct genetic target for Myc regulation in the mouse. The Bcat1 gene is highly expressed early in embryogenesis, and during organogenesis its expression is localized to the neural tube, the somites, and the mesonephric tubules. The gene is also expressed in several MYC-based tumors. Schuldiner et al. (1996) isolated and compared the structural sequences of the Bcat1 homolog in mice, human, nematode, and yeast and showed that in human, as in mouse, the BCAT1 gene is a target for MYC activity in the oncogenesis process.

[48108] It is appreciated that the abovementioned animal model for BCAT1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

[48109] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48110] Jones, C.; Moore, E. E. : Isolation of mutants lacking branched-chain amino acid transaminase. *Somat. Cell Genet.* 2: 235–243, 1976. ; and

[48111] Schuldiner, O.; Eden, A.; Ben-Yosef, T.; Yanuka, O.; Simchen, G.; Benvenisty, N. : ECA39, a conserved gene regulated by c-Myc in mice, is involved in G1/S cell cycle regulation in yeast.

[48112] Further studies establishing the function and utilities of BCAT1 are found in John Hopkins OMIM database record ID 113520, and in sited publications numbered 4194–4203 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TIRAP (Accession NM_052887) is another VGAM1367 host target gene. TIRAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIRAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIRAP BINDING SITE, designated SEQ ID:27475,

to the nucleotide sequence of VGAM1367 RNA, herein designated VGAM RNA, also designated SEQ ID:4078.

[48113] Another function of VGAM1367 is therefore inhibition of TIRAP (Accession NM_052887), a gene which is a adapter involved in the TLR4 signaling pathway in the innate immune response. Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIRAP. The function of TIRAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM189. BCL2-like 12 (proline rich) (BCL2L12, Accession NM_138639) is another VGAM1367 host target gene. BCL2L12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BCL2L12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L12 BINDING SITE, designated SEQ ID:28914, to the nucleotide sequence of VGAM1367 RNA, herein designated VGAM RNA, also designated SEQ ID:4078.

[48114] Another function of VGAM1367 is therefore inhibition of

BCL2-like 12 (proline rich) (BCL2L12, Accession NM_138639). Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L12. KIAA1798 (Accession XM_027074) is another VGAM1367 host target gene. KIAA1798 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1798 BINDING SITE, designated SEQ ID:30402, to the nucleotide sequence of VGAM1367 RNA, herein designated VGAM RNA, also designated SEQ ID:4078.

[48115] Another function of VGAM1367 is therefore inhibition of KIAA1798 (Accession XM_027074). Accordingly, utilities of VGAM1367 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1798. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1368 (VGAM1368) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[48116] VGAM1368 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1368 was detected is described hereinabove with reference to Figs. 1–8.

[48117] VGAM1368 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48118] VGAM1368 gene encodes a VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1368 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1368 precursor RNA is designated SEQ ID:1354, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1354 is located at position 44241 relative to the genome of Human Herpesvirus 6.

[48119] VGAM1368 precursor RNA folds onto itself, forming VGAM1368 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48120] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1368 folded precursor RNA into VGAM1368 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM1368 RNA is designated SEQ ID:4079, and is provided hereinbelow with reference to the sequence listing part.

[48121] VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1368 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48122] VGAM1368 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1368 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1368 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48123] The complementary binding of VGAM1368 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1368 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1368 host target RNA into VGAM1368 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48124] It is appreciated that VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1368 host target genes. The mRNA of each one of this plurality of VGAM1368 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1368 RNA, herein designated VGAM RNA, and which when bound by VGAM1368 RNA causes inhibition of translation of respective one or more VGAM1368 host target proteins.

[48125] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1368 gene, herein designated VGAM GENE, on one or more VGAM1368 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48126] It is yet further appreciated that a function of VGAM1368 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1368 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1368 correlate with, and may be deduced from, the identity of the host target genes which VGAM1368 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[48127] Nucleotide sequences of the VGAM1368 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1368 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1368 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1368 are further described hereinbelow with reference to Table 1.

[48128] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1368 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1368 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48129] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1368 gene, herein designated VGAM is inhibition of expression of VGAM1368 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1368 correlate with, and may be deduced from, the identity of the target genes which VGAM1368 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48130] Matrix Metalloproteinase 19 (MMP19, Accession NM_002429) is a VGAM1368 host target gene. MMP19 BINDING SITE1 and MMP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE1 and MMP19 BINDING SITE2, designated SEQ ID:8266 and SEQ ID:23071 respectively, to the nucleotide sequence of VGAM1368 RNA, herein designated VGAM RNA, also designated SEQ ID:4079.

[48131] A function of VGAM1368 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_002429). Accordingly, utilities of VGAM1368 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1369 (VGAM1369) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48132] VGAM1369 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1369 was detected is described hereinabove with reference to Figs. 1–8.

[48133] VGAM1369 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48134] VGAM1369 gene encodes a VGAM1369 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1369 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1369 precursor RNA is designated SEQ ID:1355, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1355 is located at position 50681 relative to the genome of Human Herpesvirus 6.

[48135] VGAM1369 precursor RNA folds onto itself, forming VGAM1369 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48136] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1369 folded precursor RNA into VGAM1369 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1369 RNA is designated SEQ ID:4080, and is provided hereinbelow with reference to the sequence listing part.

[48137] VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1369 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[48138] VGAM1369 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1369 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1369 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48139] The complementary binding of VGAM1369 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1369 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1369 host target RNA into VGAM1369 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48140] It is appreciated that VGAM1369 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1369 host target genes. The mRNA of each one of this plurality of VGAM1369 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1369 RNA, herein designated VGAM RNA, and which when bound by VGAM1369 RNA causes inhibition of translation of respective one or more VGAM1369 host target proteins.

[48141] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1369 gene, herein designated VGAM GENE, on one or more VGAM1369 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48142] It is yet further appreciated that a function of VGAM1369 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1369 correlate with, and may be deduced from, the identity of the host target genes which VGAM1369 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48143] Nucleotide sequences of the VGAM1369 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1369 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1369 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1369 are further
described hereinbelow with reference to Table 1.

[48144] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1369 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1369 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[48145] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1369 gene, herein designated VGAM is
inhibition of expression of VGAM1369 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1369 correlate with, and may be deduced
from, the identity of the target genes which VGAM1369
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[48146] ATP10C (Accession NM_024490) is a VGAM1369 host tar-
get gene. ATP10C BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by ATP10C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP10C BINDING SITE, designated SEQ ID:23689, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48147] A function of VGAM1369 is therefore inhibition of ATP10C (Accession NM_024490), a gene which is phosphorylated in their intermediate state, drives uphill transport of ions across membranes. Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP10C. The function of ATP10C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM801. Protein Tyrosine Phosphatase, Receptor Type, F (PTPRF, Accession NM_130440) is another VGAM1369 host target gene. PTPRF BINDING SITE1 and PTPRF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRF, corresponding to HOST TARGET binding sites such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRF BINDING SITE1 and PTPRF BINDING SITE2, designated SEQ ID:28199 and SEQ ID:8725 respectively, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48148] Another function of VGAM1369 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, F (PTPRF, Accession NM_130440), a gene which negatively regulates the insulin signaling pathway. Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRF. The function of PTPRF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1105. Cyclin M3 (CNNM3, Accession NM_017623) is another VGAM1369 host target gene. CNNM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM3 BINDING SITE, designated SEQ ID:19125, to the

nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48149] Another function of VGAM1369 is therefore inhibition of Cyclin M3 (CNNM3, Accession NM_017623). Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM3. KIAA1786 (Accession XM_038436) is another VGAM1369 host target gene. KIAA1786 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1786 BINDING SITE, designated SEQ ID:32847, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48150] Another function of VGAM1369 is therefore inhibition of KIAA1786 (Accession XM_038436). Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1786. NY-REN-41 (Accession NM_080654) is another VGAM1369 host target gene. NY-REN-41 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by NY-REN-41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-41 BINDING SITE, designated SEQ ID:27943, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48151] Another function of VGAM1369 is therefore inhibition of NY-REN-41 (Accession NM_080654). Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-41. Paralemmin (PALM, Accession NM_002579) is another VGAM1369 host target gene. PALM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PALM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PALM BINDING SITE, designated SEQ ID:8440, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48152] Another function of VGAM1369 is therefore inhibition of Paralemmin (PALM, Accession NM_002579). Accordingly,

utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PALM. PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM_015889) is another VGAM1369 host target gene. PCQAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCQAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCQAP BINDING SITE, designated SEQ ID:18034, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48153] Another function of VGAM1369 is therefore inhibition of PC2 (positive cofactor 2, multiprotein complex) Glutamine/Q-rich-associated Protein (PCQAP, Accession NM_015889). Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCQAP. LOC57019 (Accession NM_020313) is another VGAM1369 host target gene. LOC57019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by LOC57019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57019 BINDING SITE, designated SEQ ID:21569, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48154] Another function of VGAM1369 is therefore inhibition of LOC57019 (Accession NM_020313). Accordingly, utilities of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57019. LOC90485 (Accession XM_032059) is another VGAM1369 host target gene. LOC90485 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90485 BINDING SITE, designated SEQ ID:31553, to the nucleotide sequence of VGAM1369 RNA, herein designated VGAM RNA, also designated SEQ ID:4080.

[48155] Another function of VGAM1369 is therefore inhibition of LOC90485 (Accession XM_032059). Accordingly, utilities

of VGAM1369 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90485. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1370 (VGAM1370) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48156] VGAM1370 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1370 was detected is described hereinabove with reference to Figs. 1–8.

[48157] VGAM1370 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48158] VGAM1370 gene encodes a VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1370 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1370 precursor RNA is designated SEQ ID:1356, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1356 is located at position 50239 relative to the genome of Human Herpesvirus 6.

- [48159] VGAM1370 precursor RNA folds onto itself, forming VGAM1370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48160] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1370 folded precursor RNA into VGAM1370 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1370 RNA is designated SEQ ID:4081, and

is provided hereinbelow with reference to the sequence listing part.

[48161] VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1370 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[48162] VGAM1370 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1370 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1370 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48163] The complementary binding of VGAM1370 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1370 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1370 host target RNA into VGAM1370 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48164] It is appreciated that VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1370 host target genes. The mRNA of each one of this plurality of VGAM1370 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1370 RNA, herein designated VGAM RNA, and which when bound by VGAM1370 RNA causes inhibition of translation of respective one or more VGAM1370 host target proteins.

[48165] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1370 gene, herein designated VGAM GENE, on one or more VGAM1370 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48166] It is yet further appreciated that a function of VGAM1370 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1370 correlate with, and may be deduced from, the identity of the host target genes which VGAM1370 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48167] Nucleotide sequences of the VGAM1370 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1370 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1370 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1370 are further described hereinbelow with reference to Table 1.

[48168] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1370 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1370 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48169] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1370 gene, herein designated VGAM is inhibition of expression of VGAM1370 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1370 correlate with, and may be deduced from, the identity of the target genes which VGAM1370 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48170] Membrane Component, Chromosome 17, Surface Marker 2 (ovarian carcinoma antigen CA125) (M17S2, Accession NM_031858) is a VGAM1370 host target gene. M17S2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by M17S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M17S2 BINDING SITE, designated SEQ ID:25608, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48171] A function of VGAM1370 is therefore inhibition of Membrane Component, Chromosome 17, Surface Marker 2 (ovarian carcinoma antigen CA125) (M17S2, Accession NM_031858), a gene which Contains a B-box/coiled coil motif. Accordingly, utilities of VGAM1370 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with M17S2. The function of M17S2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1081. Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982) is another VGAM1370 host target gene. PIK3R3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R3 BINDING SITE, designated SEQ ID:30603, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48172] Another function of VGAM1370 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R3. Zinc Finger Protein 10 (KOX 1)

(ZNF10, Accession NM_015394) is another VGAM1370 host target gene. ZNF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF10 BINDING SITE, designated SEQ ID:17695, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48173] Another function of VGAM1370 is therefore inhibition of Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394), a gene which may function as a transcriptional regulator. Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF10. The function of ZNF10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36.DKFZP564I052 (Accession XM_039660) is another VGAM1370 host target gene. DKFZP564I052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I052,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I052 BINDING SITE, designated SEQ ID:33136, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48174] Another function of VGAM1370 is therefore inhibition of DKFZP564I052 (Accession XM_039660). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I052. FEM-2 (Accession NM_014634) is another VGAM1370 host target gene. FEM-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEM-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEM-2 BINDING SITE, designated SEQ ID:16008, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48175] Another function of VGAM1370 is therefore inhibition of FEM-2 (Accession NM_014634). Accordingly, utilities of

VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEM-2. Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM_044702) is another VGAM1370 host target gene. MYH10 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MYH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH10 BINDING SITE, designated SEQ ID:34263, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48176] Another function of VGAM1370 is therefore inhibition of Myosin, Heavy Polypeptide 10, Non-muscle (MYH10, Accession XM_044702). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH10. LOC201283 (Accession XM_017132) is another VGAM1370 host target gene. LOC201283 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC201283, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201283 BINDING SITE, designated SEQ ID:30304, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48177] Another function of VGAM1370 is therefore inhibition of LOC201283 (Accession XM_017132). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201283. LOC51321 (Accession NM_016627) is another VGAM1370 host target gene. LOC51321 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51321, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51321 BINDING SITE, designated SEQ ID:18742, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48178] Another function of VGAM1370 is therefore inhibition of LOC51321 (Accession NM_016627). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC51321. LOC91768 (Accession XM_040512) is another VGAM1370 host target gene. LOC91768 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91768 BINDING SITE, designated SEQ ID:33321, to the nucleotide sequence of VGAM1370 RNA, herein designated VGAM RNA, also designated SEQ ID:4081.

[48179] Another function of VGAM1370 is therefore inhibition of LOC91768 (Accession XM_040512). Accordingly, utilities of VGAM1370 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91768. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1371 (VGAM1371) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48180] VGAM1371 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1371 was detected is described hereinabove with reference to Figs. 1–8.

[48181] VGAM1371 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6.

VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48182] VGAM1371 gene encodes a VGAM1371 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1371 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1371 precursor RNA is designated SEQ ID:1357, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1357 is located at position 46060 relative to the genome of Human Herpesvirus 6.

[48183] VGAM1371 precursor RNA folds onto itself, forming VGAM1371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48184] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1371 folded precursor RNA into VGAM1371 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1371 RNA is designated SEQ ID:4082, and is provided hereinbelow with reference to the sequence listing part.

[48185] VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1371 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48186] VGAM1371 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1371 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1371 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48187] The complementary binding of VGAM1371 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1371 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1371 host target RNA into VGAM1371 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48188] It is appreciated that VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1371 host target genes. The mRNA of each one of this plurality of VGAM1371 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1371 RNA, herein designated VGAM RNA, and which when bound by VGAM1371 RNA causes inhibition of translation of respective one or more VGAM1371 host target proteins.

[48189] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1371 gene, herein designated VGAM GENE, on one or more VGAM1371 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48190] It is yet further appreciated that a function of VGAM1371 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1371 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM1371 correlate with, and may be deduced from, the identity of the host target genes which VGAM1371 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48191] Nucleotide sequences of the VGAM1371 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1371 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1371 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1371 are further described hereinbelow with reference to Table 1.

[48192] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1371 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1371 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48193] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1371 gene, herein designated VGAM is inhibition of expression of VGAM1371 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1371 correlate with, and may be deduced from, the identity of the target genes which VGAM1371 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48194] KIAA0092 (Accession NM_014679) is a VGAM1371 host target gene. KIAA0092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0092, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0092 BINDING SITE, designated SEQ ID:16153, to the nucleotide sequence of VGAM1371 RNA, herein designated VGAM RNA, also designated SEQ ID:4082.

[48195] A function of VGAM1371 is therefore inhibition of KIAA0092 (Accession NM_014679). Accordingly, utilities of VGAM1371 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0092. LOC221979 (Accession XM_166540) is another VGAM1371 host target gene. LOC221979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221979 BINDING SITE, designated SEQ ID:44512, to the nucleotide sequence of VGAM1371 RNA, herein designated VGAM RNA, also designated SEQ ID:4082.

[48196] Another function of VGAM1371 is therefore inhibition of LOC221979 (Accession XM_166540). Accordingly, utilities of VGAM1371 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC221979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1372 (VGAM1372) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48197] VGAM1372 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1372 was detected is described hereinabove with reference to Figs. 1–8.

[48198] VGAM1372 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48199] VGAM1372 gene encodes a VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1372 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1372 precursor RNA is desig-

nated SEQ ID:1358, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1358 is located at position 29852 relative to the genome of Alcelaphine Herpesvirus 1.

- [48200] VGAM1372 precursor RNA folds onto itself, forming VGAM1372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48201] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1372 folded precursor RNA into VGAM1372 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1372 RNA is designated SEQ ID:4083, and is provided hereinbelow with reference to the sequence

listing part.

[48202] VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1372 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48203] VGAM1372 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1372 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1372 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48204] The complementary binding of VGAM1372 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1372 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1372 host target RNA into VGAM1372 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48205] It is appreciated that VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1372 host target genes. The mRNA of each one of this plurality of VGAM1372 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1372 RNA, herein designated VGAM

RNA, and which when bound by VGAM1372 RNA causes inhibition of translation of respective one or more VGAM1372 host target proteins.

[48206] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1372 gene, herein designated VGAM GENE, on one or more VGAM1372 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48207] It is yet further appreciated that a function of VGAM1372 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1372 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1372 correlate with, and may be deduced from, the identity of the host target genes which VGAM1372 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48208] Nucleotide sequences of the VGAM1372 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1372 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1372 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1372 are further described hereinbelow with reference to Table 1.

[48209] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1372 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1372 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48210] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1372 gene, herein designated VGAM is

inhibition of expression of VGAM1372 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1372 correlate with, and may be deduced from, the identity of the target genes which VGAM1372 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48211] ATPase, H⁺ Transporting, Lysosomal 70kDa, V1 Subunit A, Isoform 1 (ATP6V1A1, Accession NM_001690) is a VGAM1372 host target gene. ATP6V1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1A1 BINDING SITE, designated SEQ ID:7411, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48212] A function of VGAM1372 is therefore inhibition of ATPase, H⁺ Transporting, Lysosomal 70kDa, V1 Subunit A, Isoform 1 (ATP6V1A1, Accession NM_001690), a gene which is responsible for acidifying a variety of intracellular compartments in eukaryotic cells. Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ATP6V1A1. The function of ATP6V1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM827. BTG Family, Member 2 (BTG2, Accession NM_006763) is another VGAM1372 host target gene. BTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE, designated SEQ ID:13631, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48213] Another function of VGAM1372 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM_006763). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Catalase (CAT, Accession NM_001752) is another VGAM1372 host target gene. CAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAT, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAT BINDING SITE, designated SEQ ID:7488, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48214] Another function of VGAM1372 is therefore inhibition of Catalase (CAT, Accession NM_001752). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAT. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 3 (CBFA2T3, Accession NM_005187) is another VGAM1372 host target gene. CBFA2T3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T3 BINDING SITE, designated SEQ ID:11690, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48215] Another function of VGAM1372 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2;

Translocated To, 3 (CBFA2T3, Accession NM_005187). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T3. GM2 Ganglioside Activator Protein (GM2A, Accession XM_041978) is another VGAM1372 host target gene. GM2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GM2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GM2A BINDING SITE, designated SEQ ID:33657, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48216] Another function of VGAM1372 is therefore inhibition of GM2 Ganglioside Activator Protein (GM2A, Accession XM_041978). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GM2A. Mitogen-activated Protein Kinase 8 Interacting Protein 1 (MAPK8IP1, Accession NM_005456) is another VGAM1372 host target gene. MAPK8IP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MAPK8IP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK8IP1 BINDING SITE, designated SEQ ID:11941, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48217] Another function of VGAM1372 is therefore inhibition of Mitogen-activated Protein Kinase 8 Interacting Protein 1 (MAPK8IP1, Accession NM_005456). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK8IP1. Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM_046472) is another VGAM1372 host target gene. PYCR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYCR1 BINDING SITE, designated SEQ ID:34731, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48218] Another function of VGAM1372 is therefore inhibition of Pyrroline-5-carboxylate Reductase 1 (PYCR1, Accession XM_046472), a gene which catalyzes the NAD(P)H-dependent conversion of pyrroline-5-carboxylate to proline. Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYCR1. The function of PYCR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Sal-like 2 (Drosophila) (SALL2, Accession XM_033473) is another VGAM1372 host target gene. SALL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SALL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SALL2 BINDING SITE, designated SEQ ID:31937, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48219] Another function of VGAM1372 is therefore inhibition of Sal-like 2 (Drosophila) (SALL2, Accession XM_033473).

Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SALL2. Selenoprotein X, 1 (SEPX1, Accession NM_016332) is another VGAM1372 host target gene. SEPX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPX1 BINDING SITE, designated SEQ ID:18458, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48220] Another function of VGAM1372 is therefore inhibition of Selenoprotein X, 1 (SEPX1, Accession NM_016332). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPX1. FLJ11186 (Accession NM_018353) is another VGAM1372 host target gene. FLJ11186 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ11186 BINDING SITE, designated SEQ ID:20368, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48221] Another function of VGAM1372 is therefore inhibition of FLJ11186 (Accession NM_018353). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11186. KIAA0367 (Accession XM_041018) is another VGAM1372 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33428, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48222] Another function of VGAM1372 is therefore inhibition of KIAA0367 (Accession XM_041018). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA0924 (Accession NM_014897) is another VGAM1372 host target gene. KIAA0924 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0924 BINDING SITE, designated SEQ ID:17069, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48223] Another function of VGAM1372 is therefore inhibition of KIAA0924 (Accession NM_014897). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0924. KIAA1503 (Accession XM_043197) is another VGAM1372 host target gene. KIAA1503 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1503 BINDING SITE, designated SEQ ID:33915, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48224] Another function of VGAM1372 is therefore inhibition of

KIAA1503 (Accession XM_043197). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1503. Spermatid Perinuclear RNA Binding Protein (STRBP, Accession NM_018387) is another VGAM1372 host target gene. STRBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STRBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRBP BINDING SITE, designated SEQ ID:20419, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48225] Another function of VGAM1372 is therefore inhibition of Spermatid Perinuclear RNA Binding Protein (STRBP, Accession NM_018387). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRBP. LOC134266 (Accession XM_059701) is another VGAM1372 host target gene. LOC134266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC134266, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134266 BINDING SITE, designated SEQ ID:37069, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48226] Another function of VGAM1372 is therefore inhibition of LOC134266 (Accession XM_059701). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134266. LOC149506 (Accession XM_097661) is another VGAM1372 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41007, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48227] Another function of VGAM1372 is therefore inhibition of LOC149506 (Accession XM_097661). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC149506. LOC158364 (Accession XM_088546) is another VGAM1372 host target gene. LOC158364 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158364 BINDING SITE, designated SEQ ID:39815, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48228] Another function of VGAM1372 is therefore inhibition of LOC158364 (Accession XM_088546). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158364. LOC200470 (Accession XM_117235) is another VGAM1372 host target gene. LOC200470 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC200470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200470 BINDING SITE, designated SEQ ID:43310, to

the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48229] Another function of VGAM1372 is therefore inhibition of LOC200470 (Accession XM_117235). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200470. LOC201627 (Accession XM_114353) is another VGAM1372 host target gene. LOC201627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201627 BINDING SITE, designated SEQ ID:42899, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48230] Another function of VGAM1372 is therefore inhibition of LOC201627 (Accession XM_114353). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201627. LOC221042 (Accession XM_167669) is another VGAM1372 host target gene. LOC221042 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC221042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221042 BINDING SITE, designated SEQ ID:44755, to the nucleotide sequence of VGAM1372 RNA, herein designated VGAM RNA, also designated SEQ ID:4083.

[48231] Another function of VGAM1372 is therefore inhibition of LOC221042 (Accession XM_167669). Accordingly, utilities of VGAM1372 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221042. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1373 (VGAM1373) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48232] VGAM1373 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1373 was detected is described hereinabove with reference to Figs. 1-8.

[48233] VGAM1373 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48234] VGAM1373 gene encodes a VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1373 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1373 precursor RNA is designated SEQ ID:1359, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1359 is located at position 26710 relative to the genome of Alcelaphine Herpesvirus 1.

[48235] VGAM1373 precursor RNA folds onto itself, forming VGAM1373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48236] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1373 folded precursor RNA into VGAM1373 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1373 RNA is designated SEQ ID:4084, and is provided hereinbelow with reference to the sequence listing part.

[48237] VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1373 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48238] VGAM1373 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1373 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1373 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48239] The complementary binding of VGAM1373 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1373 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1373

host target RNA into VGAM1373 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48240] It is appreciated that VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1373 host target genes. The mRNA of each one of this plurality of VGAM1373 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1373 RNA, herein designated VGAM RNA, and which when bound by VGAM1373 RNA causes inhibition of translation of respective one or more VGAM1373 host target proteins.

[48241] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1373 gene, herein designated VGAM GENE, on one or more VGAM1373 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48242] It is yet further appreciated that a function of VGAM1373 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1373 correlate with, and may be deduced from, the identity of the host target genes which VGAM1373 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48243] Nucleotide sequences of the VGAM1373 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1373 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1373 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1373 are further

described hereinbelow with reference to Table 1.

[48244] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1373 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1373 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48245] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1373 gene, herein designated VGAM is inhibition of expression of VGAM1373 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1373 correlate with, and may be deduced from, the identity of the target genes which VGAM1373 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48246] Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is a VGAM1373 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of DISC1 BINDING SITE, designated SEQ ID:20741, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48247] A function of VGAM1373 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Epithelial V-like Antigen 1 (EVA1, Accession NM_005797) is another VGAM1373 host target gene. EVA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVA1 BINDING SITE, designated SEQ ID:12380, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48248] Another function of VGAM1373 is therefore inhibition of

Epithelial V-like Antigen 1 (EVA1, Accession NM_005797). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVA1. Coagulation Factor XIII, A1 Polypeptide (F13A1, Accession XM_165833) is another VGAM1373 host target gene. F13A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F13A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F13A1 BINDING SITE, designated SEQ ID:43773, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48249] Another function of VGAM1373 is therefore inhibition of Coagulation Factor XIII, A1 Polypeptide (F13A1, Accession XM_165833). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F13A1. Glycoprotein M6A (GPM6A, Accession NM_005277) is another VGAM1373 host target gene. GPM6A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPM6A, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPM6A BINDING SITE, designated SEQ ID:11780, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48250] Another function of VGAM1373 is therefore inhibition of Glycoprotein M6A (GPM6A, Accession NM_005277), a gene which may play a role in neuronal development. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPM6A. The function of GPM6A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM326. Kinesin Family Member 5C (KIF5C, Accession NM_004522) is another VGAM1373 host target gene. KIF5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF5C BINDING SITE, designated SEQ ID:10851, to the nucleotide sequence of

VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48251] Another function of VGAM1373 is therefore inhibition of Kinesin Family Member 5C (KIF5C, Accession NM_004522). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF5C. Microtubule-associated Protein 7 (MAP7, Accession NM_003980) is another VGAM1373 host target gene. MAP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP7 BINDING SITE, designated SEQ ID:10117, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48252] Another function of VGAM1373 is therefore inhibition of Microtubule-associated Protein 7 (MAP7, Accession NM_003980), a gene which Microtubule-associated protein 7; stabilizes microtubules, may help establish epithelial cell polarity. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with MAP7. The function of MAP7 has been established by previous studies. By screening a HeLa cell expression library with antisera raised against crude microtubule-binding proteins from HeLa cells, Masson and Kreis (1993) isolated cDNAs encoding MAP7, which they designated EMAP115. The predicted 749-amino acid protein has a calculated molecular mass of 84 kD, although it migrates anomalously at 115 kD by SDS-PAGE. EMAP115 contains a basic, highly charged N-terminal region that is separated from an acidic C-terminal half by a stretch of amino acids rich in proline and alanine (PAPA region). The N-terminal basic domain contains the EMAP115 microtubule-binding site. Using immunoblots, the authors determined that EMAP115 is predominantly expressed in cells of epithelial origin. Immunofluorescence and immunoelectron microscopy indicated that it is specifically associated with microtubules in HeLa cells. Overexpression of the N-terminal microtubule-binding domain in monkey fibroblasts, which do not have significant levels of endogenous EMAP115, led to stabilization of microtubules. Masson and Kreis (1993) concluded that EMAP115 is a microtubule-stabilizing protein that may play an important role

in reorganization of microtubules during polarization and differentiation of epithelial cells. Vitamin A deficiency causes a number of defects, including deficient spermatogenesis. Almost all of these defects are reversible by the administration of a vitamin A metabolite, retinoic acid (RA), which binds and activates 2 types of receptor families, RAR (e.g., RARA; 180240) and RXR (e.g., RXRA; 180245). Using gene trap mutagenesis on mouse embryonic stem (ES) cells, Komada et al. (2000) identified MAP7 as an RA-responsive gene. The gene trap insertion led to a mutation in the Map7 gene that the authors designated ROSA63. Northern blot analysis detected broad expression of a 3.4-kb Map7 transcript, as well as a testis-specific 2.5-kb transcript, in wildtype mice, with lower expression in heterozygous ROSA63 mice and no expression in homozygous ROSA63 mice, consistent with a null allele. The authors showed that RA induces Map7 expression in ES cells in vitro and in vitamin A-deficient mice in vivo. Male mice with the ROSA63 mutation, though able to copulate, were sterile and had smaller testes and epididymis than wildtype mice, while other organs were of normal size. Histologic analysis showed that ROSA63 mutant mice exhibited defective spermatogenesis, with sper-

matid deformation in the first wave of spermatogenesis and subsequent germ cell loss. Both of these abnormalities were associated with morphologically abnormal MTs in the manchette of the spermatids and in Sertoli cells. Komada et al. (2000) noted that similar defects occur in Rara knockout mice, but not in other RA receptor knockout mice.

[48253] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48254] Komada, M.; McLean, D. J.; Griswold, M. D.; Russell, L. D.; Soriano, P. : E-MAP-115, encoding a microtubule-associated protein, is a retinoic acid-inducible gene required for spermatogenesis. *Genes Dev.* 14: 1332-1342, 2000. ; and

[48255] Masson, D.; Kreis, T. E. : Identification and molecular characterization of E-MAP-115, a novel microtubule-associated protein predominantly expressed in epithelial cells. *J. Cell Biol.*

[48256] Further studies establishing the function and utilities of MAP7 are found in John Hopkins OMIM database record ID 604108, and in cited publications numbered 7059-7060 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Recombination Ac-

tivating Gene 1 (RAG1, Accession NM_000448) is another VGAM1373 host target gene. RAG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAG1 BINDING SITE, designated SEQ ID:6043, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48257] Another function of VGAM1373 is therefore inhibition of Recombination Activating Gene 1 (RAG1, Accession NM_000448). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAG1. Transcription Factor Dp-2 (E2F dimerization partner 2) (TFDP2, Accession NM_006286) is another VGAM1373 host target gene. TFDP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TFDP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFDP2 BINDING SITE, designated SEQ

ID:12974, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48258] Another function of VGAM1373 is therefore inhibition of Transcription Factor Dp-2 (E2F dimerization partner 2) (TFDP2, Accession NM_006286), a gene which is required for the progression of S-phase during the cell cycle. Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFDP2. The function of TFDP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM222. KIAA1819 (Accession XM_045716) is another VGAM1373 host target gene. KIAA1819 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1819, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1819 BINDING SITE, designated SEQ ID:34537, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48259] Another function of VGAM1373 is therefore inhibition of KIAA1819 (Accession XM_045716). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1819. MGC15619 (Accession NM_032369) is another VGAM1373 host target gene. MGC15619 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15619 BINDING SITE, designated SEQ ID:26157, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48260] Another function of VGAM1373 is therefore inhibition of MGC15619 (Accession NM_032369). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15619. LOC115294 (Accession XM_054302) is another VGAM1373 host target gene. LOC115294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115294, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115294 BINDING SITE, designated SEQ ID:36146, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48261] Another function of VGAM1373 is therefore inhibition of LOC115294 (Accession XM_054302). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115294. LOC158357 (Accession XM_088553) is another VGAM1373 host target gene. LOC158357 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158357, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158357 BINDING SITE, designated SEQ ID:39820, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48262] Another function of VGAM1373 is therefore inhibition of LOC158357 (Accession XM_088553). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158357. LOC256905 (Accession XM_173031) is another VGAM1373 host target gene. LOC256905 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256905, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256905 BINDING SITE, designated SEQ ID:46295, to the nucleotide sequence of VGAM1373 RNA, herein designated VGAM RNA, also designated SEQ ID:4084.

[48263] Another function of VGAM1373 is therefore inhibition of LOC256905 (Accession XM_173031). Accordingly, utilities of VGAM1373 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256905. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1374 (VGAM1374) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48264] VGAM1374 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1374 was detected is described hereinabove with reference to Figs. 1–8.

[48265] VGAM1374 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48266] VGAM1374 gene encodes a VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1374 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1374 precursor RNA is designated SEQ ID:1360, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1360 is located at position 27936 relative to the genome of Alcelaphine Herpesvirus 1.

[48267] VGAM1374 precursor RNA folds onto itself, forming VGAM1374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48268] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1374 folded precursor RNA into VGAM1374 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1374 RNA is designated SEQ ID:4085, and is provided hereinbelow with reference to the sequence listing part.

[48269] VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1374 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48270] VGAM1374 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1374 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1374 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48271] The complementary binding of VGAM1374 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1374 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1374 host target RNA into VGAM1374 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48272] It is appreciated that VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1374 host target genes. The mRNA of each one of this plurality of VGAM1374 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1374 RNA, herein designated VGAM RNA, and which when bound by VGAM1374 RNA causes inhibition of translation of respective one or more VGAM1374 host target proteins.

[48273] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1374 gene, herein designated VGAM GENE, on one or more VGAM1374 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48274] It is yet further appreciated that a function of VGAM1374 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1374 correlate with, and may be deduced from, the identity of the host target genes which VGAM1374 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48275] Nucleotide sequences of the VGAM1374 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1374 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1374 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1374 are further described hereinbelow with reference to Table 1.

[48276] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1374 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1374 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48277] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1374 gene, herein designated VGAM is inhibition of expression of VGAM1374 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1374 correlate with, and may be deduced from, the identity of the target genes which VGAM1374 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48278] Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083) is a VGAM1374 host target gene. CNR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNR1, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNR1 BINDING SITE, designated SEQ ID:18160, to the nucleotide sequence of VGAM1374 RNA, herein designated VGAM RNA, also designated SEQ ID:4085.

[48279] A function of VGAM1374 is therefore inhibition of Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083), a gene which is involved in the cannabinoid-induced CNS effects. Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNR1. The function of CNR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM533. Killer Cell Lectin-like Receptor Subfamily G, Member 1 (KLRG1, Accession NM_005810) is another VGAM1374 host target gene. KLRG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLRG1 BINDING SITE,

designated SEQ ID:12391, to the nucleotide sequence of VGAM1374 RNA, herein designated VGAM RNA, also designated SEQ ID:4085.

[48280] Another function of VGAM1374 is therefore inhibition of Killer Cell Lectin-like Receptor Subfamily G, Member 1 (KLRG1, Accession NM_005810), a gene which plays a role in host defense;. Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLRG1. The function of KLRG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM648.FLJ25416 (Accession NM_145018) is another VGAM1374 host target gene. FLJ25416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ25416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25416 BINDING SITE, designated SEQ ID:29623, to the nucleotide sequence of VGAM1374 RNA, herein designated VGAM RNA, also designated SEQ ID:4085.

[48281] Another function of VGAM1374 is therefore inhibition of

FLJ25416 (Accession NM_145018). Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ25416. PFTAIRES Protein Kinase 1 (PFTK1, Accession NM_012395) is another VGAM1374 host target gene. PFTK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PFTK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PFTK1 BINDING SITE, designated SEQ ID:14749, to the nucleotide sequence of VGAM1374 RNA, herein designated VGAM RNA, also designated SEQ ID:4085.

[48282] Another function of VGAM1374 is therefore inhibition of PFTAIRES Protein Kinase 1 (PFTK1, Accession NM_012395). Accordingly, utilities of VGAM1374 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PFTK1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1375 (VGAM1375) viral gene, which modulates expression of respective host tar-

get genes thereof, the function and utility of which host target genes is known in the art.

[48283] VGAM1375 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1375 was detected is described hereinabove with reference to Figs. 1–8.

[48284] VGAM1375 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48285] VGAM1375 gene encodes a VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1375 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1375 precursor RNA is designated SEQ ID:1361, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1361 is located at position 32330 relative to the genome of Alcelaphine Herpesvirus 1.

[48286] VGAM1375 precursor RNA folds onto itself, forming VGAM1375 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48287] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1375 folded precursor RNA into VGAM1375 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1375 RNA is designated SEQ ID:4086, and is provided hereinbelow with reference to the sequence listing part.

[48288] VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1375 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48289] VGAM1375 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1375 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1375 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48290] The complementary binding of VGAM1375 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1375 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1375 host target RNA into VGAM1375 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48291] It is appreciated that VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1375 host target genes. The mRNA of each one of this plurality of VGAM1375 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1375 RNA, herein designated VGAM RNA, and which when bound by VGAM1375 RNA causes inhibition of translation of respective one or more VGAM1375 host target proteins.

[48292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1375 gene, herein designated VGAM GENE, on one or more VGAM1375 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48293] It is yet further appreciated that a function of VGAM1375 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1375 correlate with, and may be deduced from, the identity of the host target genes which VGAM1375 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[48294] Nucleotide sequences of the VGAM1375 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1375 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1375 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1375 are further described hereinbelow with reference to Table 1.

[48295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1375 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1375 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48296] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1375 gene, herein designated VGAM is inhibition of expression of VGAM1375 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1375 correlate with, and may be deduced from, the identity of the target genes which VGAM1375 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48297] Solute Carrier Family 17 (anion/sugar transporter), Member 5 (SLC17A5, Accession NM_012434) is a VGAM1375 host target gene. SLC17A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC17A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC17A5 BINDING SITE, designated SEQ ID:14813, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48298] A function of VGAM1375 is therefore inhibition of Solute Carrier Family 17 (anion/sugar transporter), Member 5 (SLC17A5, Accession NM_012434), a gene which is a member of a family of anion/cation symporters. Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC17A5. The function of SLC17A5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM766. Spectrin, Beta, Non-erythrocytic 1 (SPTBN1, Accession NM_003128) is another VGAM1375 host target gene. SPTBN1 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SPTBN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTBN1 BINDING SITE, designated SEQ ID:9095, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48299] Another function of VGAM1375 is therefore inhibition of Spectrin, Beta, Non-erythrocytic 1 (SPTBN1, Accession NM_003128), a gene which seems to be involved in secretion. Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTBN1. The function of SPTBN1 has been established by previous studies. Immunochemical studies demonstrate the existence of beta-spectrin-like polypeptides in nonerythroid tissues. Watkins et al. (1988) obtained a genomic clone for nonerythroid beta-spectrin by screening a DNA library with a synthetic oligonucleotide probe corresponding to human erythroid beta-spectrin (OMIM Ref. No. 182870) cDNA. The genomic clone showed 76% homology to the erythroid beta-spectrin cDNA when translated to amino acid sequence.

Watkins et al. (1988) used the genomic clone to map the gene to human chromosome 2 by study of DNA from somatic cell hybrids. Chang et al. (1993) found that the genomic DNA for human brain beta-fodrin contained regions that cross-hybridized with an erythroid beta-spectrin cDNA probe and that the DNA sequence of these regions showed a high degree of identity and a similar exon/intron organization. By hybridization to DNA of a panel of somatic hybrid cell lines, they mapped the gene to chromosome 2 and localized the gene to 2p21 by isotopic in situ hybridization.

[48300] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48301] Chang, J. G.; Scarpa, A.; Eddy, R. L.; Byers, M. G.; Harris, A. S.; Morrow, J. S.; Watkins, P.; Shows, T. B.; Forget, B. G. : Cloning of a portion of the chromosomal gene and cDNA for human beta-fodrin, the nonerythroid form of beta-spectrin. *Genomics* 17: 287-293, 1993. ; and

[48302] Watkins, P. C.; Eddy, R.; Forget, B. G.; Chang, J. G.; Rochelle, R.; Shows, T. B. : Assignment of a non-erythroid spectrin gene to human chromosome 2. (Abstract) *Am. J. Hum. Genet.* 43: A16.

[48303] Further studies establishing the function and utilities of SPTBN1 are found in John Hopkins OMIM database record ID 182790, and in cited publications numbered 10090–10091 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Thymidine Kinase 2, Mitochondrial (TK2, Accession NM_004614) is another VGAM1375 host target gene. TK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TK2 BINDING SITE, designated SEQ ID:10957, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48304] Another function of VGAM1375 is therefore inhibition of Thymidine Kinase 2, Mitochondrial (TK2, Accession NM_004614), a gene which phosphorylates thymidine, deoxycytidine, deoxyuridine, and also anti-viral and anti-cancer nucleoside analogs. Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TK2. The function of TK2 and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM210.CBCIP2 (Accession NM_032831) is another VGAM1375 host target gene. CBCIP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CBCIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBCIP2 BINDING SITE, designated SEQ ID:26605, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48305] Another function of VGAM1375 is therefore inhibition of CBCIP2 (Accession NM_032831). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBCIP2. Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734) is another VGAM1375 host target gene. DCAMKL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DCAMKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of DCAMKL1 BINDING SITE, designated SEQ ID:11116, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48306] Another function of VGAM1375 is therefore inhibition of Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCAMKL1. DKFZp761F2014 (Accession NM_020215) is another VGAM1375 host target gene. DKFZp761F2014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761F2014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761F2014 BINDING SITE, designated SEQ ID:21460, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48307] Another function of VGAM1375 is therefore inhibition of DKFZp761F2014 (Accession NM_020215). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp761F2014. ElaC Homolog 1 (E. coli) (ELAC1, Accession XM_165659) is another VGAM1375 host target gene. ELAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELAC1 BINDING SITE, designated SEQ ID:43722, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48308] Another function of VGAM1375 is therefore inhibition of ElaC Homolog 1 (E. coli) (ELAC1, Accession XM_165659). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELAC1. FLJ00007 (Accession XM_048928) is another VGAM1375 host target gene. FLJ00007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00007 BINDING SITE, designated SEQ

ID:35306, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48309] Another function of VGAM1375 is therefore inhibition of FLJ00007 (Accession XM_048928). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00007. FLJ14768 (Accession NM_032836) is another VGAM1375 host target gene. FLJ14768 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14768 BINDING SITE, designated SEQ ID:26614, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48310] Another function of VGAM1375 is therefore inhibition of FLJ14768 (Accession NM_032836). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14768. GFR (Accession NM_012294) is another VGAM1375 host target gene. GFR BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14632, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48311] Another function of VGAM1375 is therefore inhibition of GFR (Accession NM_012294). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. KIAA0346 (Accession XM_043272) is another VGAM1375 host target gene. KIAA0346 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0346 BINDING SITE, designated SEQ ID:33919, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48312] Another function of VGAM1375 is therefore inhibition of

KIAA0346 (Accession XM_043272). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0346. KIAA1327 (Accession XM_051146) is another VGAM1375 host target gene. KIAA1327 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1327 BINDING SITE, designated SEQ ID:35762, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48313] Another function of VGAM1375 is therefore inhibition of KIAA1327 (Accession XM_051146). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1327. P17.3 (Accession NM_019056) is another VGAM1375 host target gene. P17.3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P17.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of P17.3 BINDING SITE, designated SEQ ID:21139, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48314] Another function of VGAM1375 is therefore inhibition of P17.3 (Accession NM_019056). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P17.3. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737) is another VGAM1375 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16390, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48315] Another function of VGAM1375 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with RASSF2. Testis Expressed Sequence 27 (TEX27, Accession NM_021943) is another VGAM1375 host target gene. TEX27 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEX27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEX27 BINDING SITE, designated SEQ ID:22458, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48316] Another function of VGAM1375 is therefore inhibition of Testis Expressed Sequence 27 (TEX27, Accession NM_021943). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEX27. VI (Accession NM_013443) is another VGAM1375 host target gene. VI BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

VI BINDING SITE, designated SEQ ID:15106, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48317] Another function of VGAM1375 is therefore inhibition of VI (Accession NM_013443). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VI. LOC150935 (Accession XM_087049) is another VGAM1375 host target gene. LOC150935 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150935 BINDING SITE, designated SEQ ID:39017, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48318] Another function of VGAM1375 is therefore inhibition of LOC150935 (Accession XM_087049). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150935. LOC196955 (Accession XM_085210) is another VGAM1375 host target gene. LOC196955 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37928, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48319] Another function of VGAM1375 is therefore inhibition of LOC196955 (Accession XM_085210). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC222008 (Accession XM_168361) is another VGAM1375 host target gene. LOC222008 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC222008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222008 BINDING SITE, designated SEQ ID:45122, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48320] Another function of VGAM1375 is therefore inhibition of

LOC222008 (Accession XM_168361). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222008. LOC57805 (Accession NM_021174) is another VGAM1375 host target gene. LOC57805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57805 BINDING SITE, designated SEQ ID:22149, to the nucleotide sequence of VGAM1375 RNA, herein designated VGAM RNA, also designated SEQ ID:4086.

[48321] Another function of VGAM1375 is therefore inhibition of LOC57805 (Accession NM_021174). Accordingly, utilities of VGAM1375 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57805. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1376 (VGAM1376) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[48322] VGAM1376 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1376 was detected is described hereinabove with reference to Figs. 1–8.

[48323] VGAM1376 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48324] VGAM1376 gene encodes a VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1376 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1376 precursor RNA is designated SEQ ID:1362, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1362 is located at position 28622 relative to the genome of Alcelaphine Herpesvirus 1.

[48325] VGAM1376 precursor RNA folds onto itself, forming VGAM1376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48326] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1376 folded precursor RNA into VGAM1376 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1376 RNA is designated SEQ ID:4087, and is provided hereinbelow with reference to the sequence listing part.

[48327] VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1376 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[48328] VGAM1376 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1376 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1376 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[48329] The complementary binding of VGAM1376 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1376 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1376 host target RNA into VGAM1376 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48330] It is appreciated that VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1376 host target genes. The mRNA of each one of this plurality of VGAM1376 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1376 RNA, herein designated VGAM RNA, and which when bound by VGAM1376 RNA causes inhibition of translation of respective one or more VGAM1376 host target proteins.

[48331] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1376 gene, herein designated VGAM GENE, on one

or more VGAM1376 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48332] It is yet further appreciated that a function of VGAM1376 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1376 correlate with, and may be deduced from, the identity of the host target genes which VGAM1376 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48333] Nucleotide sequences of the VGAM1376 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1376 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1376 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1376 are further described hereinbelow with reference to Table 1.

[48334] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1376 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1376 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48335] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1376 gene, herein designated VGAM is inhibition of expression of VGAM1376 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1376 correlate with, and may be deduced from, the identity of the target genes which VGAM1376 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48336] Transcobalamin II; Macrocytic Anemia (TCN2, Accession

NM_000355) is a VGAM1376 host target gene. TCN2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCN2 BINDING SITE, designated SEQ ID:5915, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48337] A function of VGAM1376 is therefore inhibition of Transcobalamin II; Macrocytic Anemia (TCN2, Accession NM_000355). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCN2. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621) is another VGAM1376 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10974, to the nucleotide sequence of VGAM1376 RNA,

herein designated VGAM RNA, also designated SEQ ID:4087.

[48338] Another function of VGAM1376 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25.DKFZP434F091 (Accession NM_015453) is another VGAM1376 host target gene. DKFZP434F091 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434F091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F091 BINDING SITE, designated SEQ ID:17738, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48339] Another function of VGAM1376 is therefore inhibition of

DKFZP434F091 (Accession NM_015453). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F091. FLJ23132 (Accession XM_171194) is another VGAM1376 host target gene. FLJ23132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23132 BINDING SITE, designated SEQ ID:45981, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48340] Another function of VGAM1376 is therefore inhibition of FLJ23132 (Accession XM_171194). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23132. Netrin 4 (NTN4, Accession XM_031896) is another VGAM1376 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of NTN4 BINDING SITE, designated SEQ ID:31512, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48341] Another function of VGAM1376 is therefore inhibition of Netrin 4 (NTN4, Accession XM_031896). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. SEC61A1 (Accession NM_013336) is another VGAM1376 host target gene. SEC61A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEC61A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC61A1 BINDING SITE, designated SEQ ID:14984, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48342] Another function of VGAM1376 is therefore inhibition of SEC61A1 (Accession NM_013336). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC61A1. TGFB-induced Factor 2 (TALE family homeobox)

(TGIF2, Accession NM_021809) is another VGAM1376 host target gene. TGIF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGIF2 BINDING SITE, designated SEQ ID:22365, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48343] Another function of VGAM1376 is therefore inhibition of TGFB-induced Factor 2 (TALE family homeobox) (TGIF2, Accession NM_021809). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGIF2. LOC145098 (Accession XM_085022) is another VGAM1376 host target gene. LOC145098 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145098 BINDING SITE, designated SEQ ID:37796, to

the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48344] Another function of VGAM1376 is therefore inhibition of LOC145098 (Accession XM_085022). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145098. LOC145719 (Accession XM_096848) is another VGAM1376 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40572, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48345] Another function of VGAM1376 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM1376 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40562, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48346] Another function of VGAM1376 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145720. LOC155382 (Accession XM_098713) is another VGAM1376 host target gene. LOC155382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC155382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155382 BINDING SITE, designated SEQ ID:41764, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48347] Another function of VGAM1376 is therefore inhibition of LOC155382 (Accession XM_098713). Accordingly, utilities

of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155382. LOC197114 (Accession XM_116987) is another VGAM1376 host target gene. LOC197114 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197114 BINDING SITE, designated SEQ ID:43186, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48348] Another function of VGAM1376 is therefore inhibition of LOC197114 (Accession XM_116987). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197114. LOC254013 (Accession XM_170700) is another VGAM1376 host target gene. LOC254013 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC254013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC254013 BINDING SITE, designated SEQ ID:45479, to the nucleotide sequence of VGAM1376 RNA, herein designated VGAM RNA, also designated SEQ ID:4087.

[48349] Another function of VGAM1376 is therefore inhibition of LOC254013 (Accession XM_170700). Accordingly, utilities of VGAM1376 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254013. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1377 (VGAM1377) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48350] VGAM1377 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1377 was detected is described hereinabove with reference to Figs. 1–8.

[48351] VGAM1377 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48352] VGAM1377 gene encodes a VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1377 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1377 precursor RNA is designated SEQ ID:1363, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1363 is located at position 27042 relative to the genome of Alcelaphine Herpesvirus 1.

[48353] VGAM1377 precursor RNA folds onto itself, forming VGAM1377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48354] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1377 folded precursor RNA into VGAM1377 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1377 RNA is designated SEQ ID:4088, and is provided hereinbelow with reference to the sequence listing part.

[48355] VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1377 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48356] VGAM1377 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1377 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1377 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48357] The complementary binding of VGAM1377 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1377 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1377 host target RNA into VGAM1377 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48358] It is appreciated that VGAM1377 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1377 host target genes. The mRNA of each one of this plurality of VGAM1377 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1377 RNA, herein designated VGAM RNA, and which when bound by VGAM1377 RNA causes inhibition of translation of respective one or more VGAM1377 host target proteins.

[48359] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1377 gene, herein designated VGAM GENE, on one or more VGAM1377 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[48360] It is yet further appreciated that a function of VGAM1377 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1377 correlate with, and may be deduced from, the identity of the host target genes which VGAM1377 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48361] Nucleotide sequences of the VGAM1377 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1377 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1377 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1377 are further described hereinbelow with reference to Table 1.

[48362] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1377 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1377 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48363] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1377 gene, herein designated VGAM is inhibition of expression of VGAM1377 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1377 correlate with, and may be deduced from, the identity of the target genes which VGAM1377 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48364] Coronin, Actin Binding Protein, 2A (CORO2A, Accession NM_003389) is a VGAM1377 host target gene. CORO2A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CORO2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CORO2A BINDING SITE, designated SEQ ID:9426, to the nucleotide sequence of VGAM1377 RNA, herein designated VGAM RNA, also designated SEQ ID:4088.

[48365] A function of VGAM1377 is therefore inhibition of Coronin, Actin Binding Protein, 2A (CORO2A, Accession NM_003389). Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CORO2A. Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM_016255) is another VGAM1377 host target gene. FAM8A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FAM8A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAM8A1 BINDING SITE, designated SEQ ID:18383, to the nucleotide sequence of VGAM1377 RNA, herein designated VGAM RNA, also designated SEQ ID:4088.

[48366] Another function of VGAM1377 is therefore inhibition of Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM_016255). Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAM8A1. FLJ22843 (Accession NM_025184) is another VGAM1377 host target gene. FLJ22843 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22843 BINDING SITE, designated SEQ ID:24821, to the nucleotide sequence of VGAM1377 RNA, herein designated VGAM RNA, also designated SEQ ID:4088.

[48367] Another function of VGAM1377 is therefore inhibition of FLJ22843 (Accession NM_025184). Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22843. LOC200310 (Accession XM_037840) is another VGAM1377 host target gene. LOC200310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200310 BINDING SITE, designated SEQ ID:32707, to the nucleotide sequence of VGAM1377 RNA, herein designated VGAM RNA, also designated SEQ ID:4088.

[48368] Another function of VGAM1377 is therefore inhibition of

LOC200310 (Accession XM_037840). Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200310. LOC90625 (Accession XM_033004) is another VGAM1377 host target gene. LOC90625 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90625 BINDING SITE, designated SEQ ID:31820, to the nucleotide sequence of VGAM1377 RNA, herein designated VGAM RNA, also designated SEQ ID:4088.

[48369] Another function of VGAM1377 is therefore inhibition of LOC90625 (Accession XM_033004). Accordingly, utilities of VGAM1377 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90625. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1378 (VGAM1378) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[48370] VGAM1378 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1378 was detected is described hereinabove with reference to Figs. 1–8.

[48371] VGAM1378 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 1. VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48372] VGAM1378 gene encodes a VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1378 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1378 precursor RNA is designated SEQ ID:1364, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1364 is located at position 141854 relative to the genome of Human Herpesvirus 1.

[48373] VGAM1378 precursor RNA folds onto itself, forming VGAM1378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48374] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1378 folded precursor RNA into VGAM1378 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1378 RNA is designated SEQ ID:4089, and is provided hereinbelow with reference to the sequence listing part.

[48375] VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1378 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[48376] VGAM1378 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1378 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1378 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[48377] The complementary binding of VGAM1378 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1378 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1378 host target RNA into VGAM1378 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48378] It is appreciated that VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1378 host target genes. The mRNA of each one of this plurality of VGAM1378 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1378 RNA, herein designated VGAM RNA, and which when bound by VGAM1378 RNA causes inhibition of translation of respective one or more VGAM1378 host target proteins.

[48379] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1378 gene, herein designated VGAM GENE, on one

or more VGAM1378 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48380] It is yet further appreciated that a function of VGAM1378 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1378 correlate with, and may be deduced from, the identity of the host target genes which VGAM1378 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48381] Nucleotide sequences of the VGAM1378 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1378 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1378 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1378 are further described hereinbelow with reference to Table 1.

[48382] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1378 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1378 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48383] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1378 gene, herein designated VGAM is inhibition of expression of VGAM1378 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1378 correlate with, and may be deduced from, the identity of the target genes which VGAM1378 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48384] Axin 1 (AXIN1, Accession XM_027520) is a VGAM1378

host target gene. AXIN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AXIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AXIN1 BINDING SITE, designated SEQ ID:30517, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48385] A function of VGAM1378 is therefore inhibition of Axin 1 (AXIN1, Accession XM_027520). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AXIN1. Calbindin 1, 28kDa (CALB1, Accession NM_004929) is another VGAM1378 host target gene. CALB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALB1 BINDING SITE, designated SEQ ID:11368, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48386] Another function of VGAM1378 is therefore inhibition of Calbindin 1, 28kDa (CALB1, Accession NM_004929), a gene which buffers cytosolic calcium. Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALB1. The function of CALB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM266. Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM_033096) is another VGAM1378 host target gene. CLTCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLTCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLTCL1 BINDING SITE, designated SEQ ID:31834, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48387] Another function of VGAM1378 is therefore inhibition of Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM_033096), a gene which is involved in vesicle budding. Accordingly, utilities of VGAM1378 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with CLTCL1. The function of CLTCL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM42. EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883) is another VGAM1378 host target gene.

EGFL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30961, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48388] Another function of VGAM1378 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL4. Exostoses (multiple)-like 3 (EXTL3, Accession NM_001440) is another VGAM1378 host target gene. EXTL3 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7169, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48389] Another function of VGAM1378 is therefore inhibition of Exostoses (multiple)-like 3 (EXTL3, Accession NM_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Low Density Lipoprotein-related Protein 1 (alpha-2-macroglobulin receptor) (LRP1, Accession NM_002332) is another VGAM1378 host target gene. LRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP1, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP1 BINDING SITE, designated SEQ ID:8138, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48390] Another function of VGAM1378 is therefore inhibition of Low Density Lipoprotein-related Protein 1 (alpha-2-macroglobulin receptor) (LRP1, Accession NM_002332), a gene which is a recycling lipoprotein receptor with possible growth-modulating effects. Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP1. The function of LRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM_166424) is another VGAM1378 host target gene. PACSIN1 BINDING SITE1 and PACSIN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PACSIN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementar-

ity of the nucleotide sequences of PACSIN1 BINDING SITE1 and PACSIN1 BINDING SITE2, designated SEQ ID:44312 and SEQ ID:44313 respectively, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48391] Another function of VGAM1378 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 1 (PACSIN1, Accession XM_166424). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN1. FLJ14124 (Accession NM_024868) is another VGAM1378 host target gene. FLJ14124 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14124, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14124 BINDING SITE, designated SEQ ID:24303, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48392] Another function of VGAM1378 is therefore inhibition of FLJ14124 (Accession NM_024868). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14124. FLJ20413 (Accession NM_017808) is another VGAM1378 host target gene. FLJ20413 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20413, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20413 BINDING SITE, designated SEQ ID:19451, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48393] Another function of VGAM1378 is therefore inhibition of FLJ20413 (Accession NM_017808). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20413. IL-17RC (Accession NM_032732) is another VGAM1378 host target gene. IL-17RC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL-17RC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL-17RC BINDING SITE, designated SEQ ID:26455, to the nucleotide

sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48394] Another function of VGAM1378 is therefore inhibition of IL-17RC (Accession NM_032732). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL-17RC. KIAA0876 (Accession XM_035625) is another VGAM1378 host target gene. KIAA0876 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0876 BINDING SITE, designated SEQ ID:32293, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48395] Another function of VGAM1378 is therefore inhibition of KIAA0876 (Accession XM_035625). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0876. KIAA1576 (Accession XM_038186) is another VGAM1378 host target gene. KIAA1576 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1576 BINDING SITE, designated SEQ ID:32774, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48396] Another function of VGAM1378 is therefore inhibition of KIAA1576 (Accession XM_038186). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1576. PP1201 (Accession NM_022152) is another VGAM1378 host target gene. PP1201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1201 BINDING SITE, designated SEQ ID:22711, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48397] Another function of VGAM1378 is therefore inhibition of PP1201 (Accession NM_022152). Accordingly, utilities of

VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1201. WD Repeat Domain 7 (WDR7, Accession NM_015285) is another VGAM1378 host target gene. WDR7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by WDR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR7 BINDING SITE, designated SEQ ID:17608, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48398] Another function of VGAM1378 is therefore inhibition of WD Repeat Domain 7 (WDR7, Accession NM_015285). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR7. LOC149076 (Accession XM_086415) is another VGAM1378 host target gene. LOC149076 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149076, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC149076 BINDING SITE, designated SEQ ID:38637, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48399] Another function of VGAM1378 is therefore inhibition of LOC149076 (Accession XM_086415). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149076. LOC199920 (Accession XM_114056) is another VGAM1378 host target gene. LOC199920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199920 BINDING SITE, designated SEQ ID:42661, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48400] Another function of VGAM1378 is therefore inhibition of LOC199920 (Accession XM_114056). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199920. LOC200470 (Accession XM_117235) is an-

other VGAM1378 host target gene. LOC200470 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200470 BINDING SITE, designated SEQ ID:43307, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48401] Another function of VGAM1378 is therefore inhibition of LOC200470 (Accession XM_117235). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200470. LOC220097 (Accession XM_167887) is another VGAM1378 host target gene. LOC220097 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220097 BINDING SITE, designated SEQ ID:44896, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48402] Another function of VGAM1378 is therefore inhibition of LOC220097 (Accession XM_167887). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220097. LOC222031 (Accession XM_168371) is another VGAM1378 host target gene. LOC222031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222031 BINDING SITE, designated SEQ ID:45135, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48403] Another function of VGAM1378 is therefore inhibition of LOC222031 (Accession XM_168371). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222031. LOC90979 (Accession XM_035323) is another VGAM1378 host target gene. LOC90979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90979, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90979 BINDING SITE, designated SEQ ID:32231, to the nucleotide sequence of VGAM1378 RNA, herein designated VGAM RNA, also designated SEQ ID:4089.

[48404] Another function of VGAM1378 is therefore inhibition of LOC90979 (Accession XM_035323). Accordingly, utilities of VGAM1378 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1379 (VGAM1379) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48405] VGAM1379 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1379 was detected is described hereinabove with reference to Figs. 1-8.

[48406] VGAM1379 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 1. VGAM1379 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[48407] VGAM1379 gene encodes a VGAM1379 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1379 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1379 precursor RNA is designated SEQ ID:1365, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1365 is located at position 142746 relative to the genome of Human Herpesvirus 1.

[48408] VGAM1379 precursor RNA folds onto itself, forming VGAM1379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48409] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1379 folded precursor RNA into VGAM1379

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1379 RNA is designated SEQ ID:4090, and is provided hereinbelow with reference to the sequence listing part.

[48410] VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1379 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48411] VGAM1379 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1379 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1379 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48412] The complementary binding of VGAM1379 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1379 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1379 host target RNA into VGAM1379 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[48413] It is appreciated that VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1379 host target genes. The mRNA of each one of this plurality of VGAM1379 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1379 RNA, herein designated VGAM RNA, and which when bound by VGAM1379 RNA causes inhibition of translation of respective one or more VGAM1379 host target proteins.

[48414] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1379 gene, herein designated VGAM GENE, on one or more VGAM1379 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48415] It is yet further appreciated that a function of VGAM1379 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1379 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1379 correlate with, and may be deduced from, the identity of the host target genes which VGAM1379 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48416] Nucleotide sequences of the VGAM1379 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1379 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1379 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1379 are further described hereinbelow with reference to Table 1.

[48417] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1379 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1379 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48418] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1379 gene, herein designated VGAM is inhibition of expression of VGAM1379 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1379 correlate with, and may be deduced from, the identity of the target genes which VGAM1379 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48419] KIAA1322 (Accession XM_052626) is a VGAM1379 host target gene. KIAA1322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1322 BINDING SITE, designated SEQ ID:36025, to the nucleotide sequence of VGAM1379 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4090.

[48420] A function of VGAM1379 is therefore inhibition of KIAA1322 (Accession XM_052626). Accordingly, utilities of VGAM1379 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1322. TIP120B (Accession XM_051590) is another VGAM1379 host target gene. TIP120B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIP120B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIP120B BINDING SITE, designated SEQ ID:35859, to the nucleotide sequence of VGAM1379 RNA, herein designated VGAM RNA, also designated SEQ ID:4090.

[48421] Another function of VGAM1379 is therefore inhibition of TIP120B (Accession XM_051590). Accordingly, utilities of VGAM1379 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIP120B. LOC120448 (Accession XM_062032) is another VGAM1379 host target gene. LOC120448 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120448, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120448 BINDING SITE, designated SEQ ID:37222, to the nucleotide sequence of VGAM1379 RNA, herein designated VGAM RNA, also designated SEQ ID:4090.

[48422] Another function of VGAM1379 is therefore inhibition of LOC120448 (Accession XM_062032). Accordingly, utilities of VGAM1379 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120448. LOC256158 (Accession XM_175125) is another VGAM1379 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46627, to the nucleotide sequence of VGAM1379 RNA, herein designated VGAM RNA, also designated SEQ ID:4090.

[48423] Another function of VGAM1379 is therefore inhibition of LOC256158 (Accession XM_175125). Accordingly, utilities of VGAM1379 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC256158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1380 (VGAM1380) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48424] VGAM1380 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1380 was detected is described hereinabove with reference to Figs. 1–8.

[48425] VGAM1380 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus. VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48426] VGAM1380 gene encodes a VGAM1380 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1380 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1380 precursor RNA is desig-

nated SEQ ID:1366, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1366 is located at position 2325 relative to the genome of Himetobi P Virus.

- [48427] VGAM1380 precursor RNA folds onto itself, forming VGAM1380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48428] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1380 folded precursor RNA into VGAM1380 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1380 RNA is designated SEQ ID:4091, and is provided hereinbelow with reference to the sequence

listing part.

[48429] VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1380 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48430] VGAM1380 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1380 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1380 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48431] The complementary binding of VGAM1380 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1380 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1380 host target RNA into VGAM1380 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48432] It is appreciated that VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1380 host target genes. The mRNA of each one of this plurality of VGAM1380 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1380 RNA, herein designated VGAM

RNA, and which when bound by VGAM1380 RNA causes inhibition of translation of respective one or more VGAM1380 host target proteins.

[48433] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1380 gene, herein designated VGAM GENE, on one or more VGAM1380 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48434] It is yet further appreciated that a function of VGAM1380 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1380 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1380 correlate with, and may be deduced from, the identity of the host target genes which VGAM1380 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48435] Nucleotide sequences of the VGAM1380 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1380 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1380 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1380 are further described hereinbelow with reference to Table 1.

[48436] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1380 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1380 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48437] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1380 gene, herein designated VGAM is

inhibition of expression of VGAM1380 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1380 correlate with, and may be deduced from, the identity of the target genes which VGAM1380 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48438] FENS-1 (Accession NM_020830) is a VGAM1380 host target gene. FENS-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FENS-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FENS-1 BINDING SITE, designated SEQ ID:21894, to the nucleotide sequence of VGAM1380 RNA, herein designated VGAM RNA, also designated SEQ ID:4091.

[48439] A function of VGAM1380 is therefore inhibition of FENS-1 (Accession NM_020830). Accordingly, utilities of VGAM1380 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FENS-1. PRO0902 (Accession NM_053057) is another VGAM1380 host target gene. PRO0902 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by PRO0902, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0902 BINDING SITE, designated SEQ ID:27604, to the nucleotide sequence of VGAM1380 RNA, herein designated VGAM RNA, also designated SEQ ID:4091.

[48440] Another function of VGAM1380 is therefore inhibition of PRO0902 (Accession NM_053057). Accordingly, utilities of VGAM1380 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0902. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1381 (VGAM1381) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48441] VGAM1381 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1381 was detected is described hereinabove with reference to Figs. 1-8.

[48442] VGAM1381 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Himetobi P Virus.

VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48443] VGAM1381 gene encodes a VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1381 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1381 precursor RNA is designated SEQ ID:1367, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1367 is located at position 8357 relative to the genome of Himetobi P Virus.

[48444] VGAM1381 precursor RNA folds onto itself, forming VGAM1381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48445] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1381 folded precursor RNA into VGAM1381 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1381 RNA is designated SEQ ID:4092, and is provided hereinbelow with reference to the sequence listing part.

[48446] VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1381 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48447] VGAM1381 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1381 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1381 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48448] The complementary binding of VGAM1381 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1381 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1381

host target RNA into VGAM1381 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48449] It is appreciated that VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1381 host target genes. The mRNA of each one of this plurality of VGAM1381 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1381 RNA, herein designated VGAM RNA, and which when bound by VGAM1381 RNA causes inhibition of translation of respective one or more VGAM1381 host target proteins.

[48450] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1381 gene, herein designated VGAM GENE, on one or more VGAM1381 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48451] It is yet further appreciated that a function of VGAM1381 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1381 correlate with, and may be deduced from, the identity of the host target genes which VGAM1381 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48452] Nucleotide sequences of the VGAM1381 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1381 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1381 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1381 are further

described hereinbelow with reference to Table 1.

[48453] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1381 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1381 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48454] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1381 gene, herein designated VGAM is inhibition of expression of VGAM1381 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1381 correlate with, and may be deduced from, the identity of the target genes which VGAM1381 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48455] RAB1A, Member RAS Oncogene Family (RAB1A, Accession XM_046674) is a VGAM1381 host target gene. RAB1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of RAB1A BINDING SITE, designated SEQ ID:34786, to the nucleotide sequence of VGAM1381 RNA, herein designated VGAM RNA, also designated SEQ ID:4092.

[48456] A function of VGAM1381 is therefore inhibition of RAB1A, Member RAS Oncogene Family (RAB1A, Accession XM_046674), a gene which is involved in vesicle transport. Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB1A. The function of RAB1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.KIAA0367 (Accession XM_041018) is another VGAM1381 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33422, to the nucleotide sequence of VGAM1381 RNA, herein designated VGAM RNA, also designated SEQ ID:4092.

[48457] Another function of VGAM1381 is therefore inhibition of

KIAA0367 (Accession XM_041018). Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA1030 (Accession XM_167789) is another VGAM1381 host target gene. KIAA1030 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1030, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1030 BINDING SITE, designated SEQ ID:44816, to the nucleotide sequence of VGAM1381 RNA, herein designated VGAM RNA, also designated SEQ ID:4092.

[48458] Another function of VGAM1381 is therefore inhibition of KIAA1030 (Accession XM_167789). Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1030. LOC162239 (Accession XM_091439) is another VGAM1381 host target gene. LOC162239 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC162239, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC162239 BINDING SITE, designated SEQ ID:40050, to the nucleotide sequence of VGAM1381 RNA, herein designated VGAM RNA, also designated SEQ ID:4092.

[48459] Another function of VGAM1381 is therefore inhibition of LOC162239 (Accession XM_091439). Accordingly, utilities of VGAM1381 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162239. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1382 (VGAM1382) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48460] VGAM1382 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1382 was detected is described hereinabove with reference to Figs. 1–8.

[48461] VGAM1382 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus. VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[48462] VGAM1382 gene encodes a VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1382 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1382 precursor RNA is designated SEQ ID:1368, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1368 is located at position 4080 relative to the genome of Himetobi P Virus.

[48463] VGAM1382 precursor RNA folds onto itself, forming VGAM1382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48464] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1382 folded precursor RNA into VGAM1382 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1382 RNA is designated SEQ ID:4093, and is provided hereinbelow with reference to the sequence listing part.

[48465] VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1382 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48466] VGAM1382 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1382 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1382 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48467] The complementary binding of VGAM1382 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1382 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1382 host target RNA into VGAM1382 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48468] It is appreciated that VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1382 host target genes. The mRNA of each one of this plurality of VGAM1382 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1382 RNA, herein designated VGAM RNA, and which when bound by VGAM1382 RNA causes inhibition of translation of respective one or more VGAM1382 host target proteins.

[48469] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1382 gene, herein designated VGAM GENE, on one or more VGAM1382 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48470] It is yet further appreciated that a function of VGAM1382 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1382 correlate with, and may be deduced from, the identity of the host target genes which VGAM1382 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48471] Nucleotide sequences of the VGAM1382 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1382 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1382 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1382 are further described hereinbelow with reference to Table 1.

[48472] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1382 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1382 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48473] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1382 gene, herein designated VGAM is inhibition of expression of VGAM1382 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1382 correlate with, and may be deduced from, the identity of the target genes which VGAM1382 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48474] Active BCR-related Gene (ABR, Accession NM_001092) is a VGAM1382 host target gene. ABR BINDING SITE1 and ABR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABR BINDING SITE1 and ABR BINDING SITE2, designated SEQ ID:6751 and SEQ ID:22496 respectively, to the nucleotide sequence of VGAM1382 RNA, herein designated

VGAM RNA, also designated SEQ ID:4093.

[48475] A function of VGAM1382 is therefore inhibition of Active BCR-related Gene (ABR, Accession NM_001092), a gene which gtpase-activating protein for rac and cdc42. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABR. The function of ABR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM489. Cell Matrix Adhesion Regulator (CMAR, Accession NM_005200) is another VGAM1382 host target gene. CMAR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CMAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMAR BINDING SITE, designated SEQ ID:11699, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48476] Another function of VGAM1382 is therefore inhibition of Cell Matrix Adhesion Regulator (CMAR, Accession NM_005200). Accordingly, utilities of VGAM1382 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CMAR. Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083) is another VGAM1382 host target gene. CNR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNR1 BINDING SITE, designated SEQ ID:18163, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48477] Another function of VGAM1382 is therefore inhibition of Cannabinoid Receptor 1 (brain) (CNR1, Accession NM_016083), a gene which is involved in the cannabinoid-induced CNS effects. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNR1. The function of CNR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM533. Cysteine-rich Motor Neuron 1 (CRIM1, Accession NM_016441) is another VGAM1382 host target

gene. CRIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRIM1 BINDING SITE, designated SEQ ID:18562, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48478] Another function of VGAM1382 is therefore inhibition of Cysteine-rich Motor Neuron 1 (CRIM1, Accession NM_016441). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRIM1. Protocadherin Alpha 1 (PCDHA1, Accession NM_031411) is another VGAM1382 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:25384 and SEQ ID:20865 respectively,

to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48479] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_031411). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_031860) is another VGAM1382 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:25616 and SEQ ID:20885 respectively, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48480] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_031860). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin

Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM1382 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20906, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48481] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM_018905) is another VGAM1382 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20916, to the nucleotide

sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48482] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM_018905). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM1382 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20926, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48483] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM1382

host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20936, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48484] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM_018908) is another VGAM1382 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20946, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4093.

[48485] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM_018908). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM_018909) is another VGAM1382 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:20956 and SEQ ID:25588 respectively, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48486] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 6 (PCDHA6, Accession NM_018909). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM_018911) is another VGAM1382

host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20976, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48487] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 8 (PCDHA8, Accession NM_018911). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM1382 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25601, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4093.

[48488] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM1382 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated SEQ ID:20845, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48489] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession

NM_018898). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899) is another VGAM1382 host target gene. PCDHAC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC2 BINDING SITE, designated SEQ ID:20855, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48490] Another function of VGAM1382 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. Phosphorylase, Glycogen; Muscle (McArdle syndrome, glycogen storage disease type V) (PYGM, Accession NM_005609) is another VGAM1382 host target gene. PYGM BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PYGM, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGM BINDING SITE, designated SEQ ID:12128, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48491] Another function of VGAM1382 is therefore inhibition of Phosphorylase, Glycogen; Muscle (McArdle syndrome, glycogen storage disease type V) (PYGM, Accession NM_005609). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGM. Spastic Paraplegia 7, Paraplegin (pure and complicated autosomal recessive) (SPG7, Accession NM_003119) is another VGAM1382 host target gene. SPG7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPG7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPG7 BINDING SITE, designated SEQ ID:9090, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48492] Another function of VGAM1382 is therefore inhibition of

Spastic Paraplegia 7, Paraplegin (pure and complicated autosomal recessive) (SPG7, Accession NM_003119), a gene which act as an atp-dependent zinc metallopeptidase. involved in the degradation of sigma-32. Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPG7. The function of SPG7 has been established by previous studies. Casari et al. (1998) determined that paraplegin is highly homologous to the yeast mitochondrial ATPases AFG3, RCA1, and YME1, which have both proteolytic and chaperone-like activities at the inner mitochondrial membrane. Immunofluorescence analysis and import experiments showed that paraplegin localizes to mitochondria. Analysis of muscle biopsies from 2 patients with paraplegin mutations showed typical signs of mitochondrial OXPHOS defects, thus suggesting a mechanism for neurodegeneration in SPG-type disorders. Based on linkage analysis of a family with autosomal recessive spastic paraplegia that mapped to 16q24.3 (SPG7; 607259), Casari et al. (1998) used an EST clone to screen a human cDNA library and isolate a candidate gene. The full-length cDNA sequence corresponding to this gene encoded a deduced 795-amino acid protein, which they

named paraplegin. Northern blot analysis detected a transcript of approximately 3.2 kb in all fetal and adult tissues tested. Two additional hybridizing transcripts of approximately 2.6 and 7.5 kb were detected in heart and pancreas

[48493] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48494] Casari, G.; De Fusco, M.; Ciarmatori, S.; Zeviani, M.; Mora, M.; Fernandez, P.; De Michele, G.; Filla, A.; Coccozza, S.; Marconi, R.; Durr, A.; Fontaine, B.; Ballabio, A. : Spastic paraplegia and OXPHOS impairment caused by mutations in paraplegin, a nuclear-encoded mitochondrial metalloprotease. Cell 93: 973–983, 1998. ; and

[48495] Casari, G.; De Fusco, M.; Ciarmatori, S.; Zeviani, M.; Mora, M.; Fernandez, P.; De Michele, G.; Filla, A.; Coccozza, S.; Marconi, R.; Durr, A.; Fontaine, B.; Ballabio, A. : Spastic paraplegi.

[48496] Further studies establishing the function and utilities of SPG7 are found in John Hopkins OMIM database record ID 602783, and in cited publications numbered 7660–7662 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chemokine (C–C

motif) Receptor 6 (CCR6, Accession NM_031409) is another VGAM1382 host target gene. CCR6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CCR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE, designated SEQ ID:25368, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48497] Another function of VGAM1382 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM_031409). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. COAS3 (Accession NM_139020) is another VGAM1382 host target gene. COAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COAS3 BINDING SITE, designated SEQ ID:29118, to the nucleotide sequence of VGAM1382 RNA,

herein designated VGAM RNA, also designated SEQ ID:4093.

[48498] Another function of VGAM1382 is therefore inhibition of COAS3 (Accession NM_139020). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COAS3. Complexin 1 (CPLX1, Accession NM_006651) is another VGAM1382 host target gene. CPLX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPLX1 BINDING SITE, designated SEQ ID:13452, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48499] Another function of VGAM1382 is therefore inhibition of Complexin 1 (CPLX1, Accession NM_006651). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPLX1. DKFZP434L1435 (Accession XM_166401) is another VGAM1382 host target gene. DKFZP434L1435 BINDING SITE is HOST TARGET binding site found in the

5` untranslated region of mRNA encoded by DKFZP434L1435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L1435 BINDING SITE, designated SEQ ID:44266, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48500] Another function of VGAM1382 is therefore inhibition of DKFZP434L1435 (Accession XM_166401). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L1435. DnaJ (Hsp40) Homolog, Subfamily C, Member 5 (DNAJC5, Accession XM_028966) is another VGAM1382 host target gene. DNAJC5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNAJC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC5 BINDING SITE, designated SEQ ID:30815, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48501] Another function of VGAM1382 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 5 (DNAJC5, Accession XM_028966). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC5. FLJ12875 (Accession NM_024544) is another VGAM1382 host target gene. FLJ12875 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12875, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12875 BINDING SITE, designated SEQ ID:23754, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48502] Another function of VGAM1382 is therefore inhibition of FLJ12875 (Accession NM_024544). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12875. FLJ13181 (Accession NM_025188) is another VGAM1382 host target gene. FLJ13181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13181, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13181 BINDING SITE, designated SEQ ID:24829, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48503] Another function of VGAM1382 is therefore inhibition of FLJ13181 (Accession NM_025188). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13181. FLJ14564 (Accession XM_084459) is another VGAM1382 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564 BINDING SITE, designated SEQ ID:37596, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48504] Another function of VGAM1382 is therefore inhibition of FLJ14564 (Accession XM_084459). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14564. FLJ14800 (Accession NM_032840) is another VGAM1382 host target gene. FLJ14800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14800 BINDING SITE, designated SEQ ID:26623, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48505] Another function of VGAM1382 is therefore inhibition of FLJ14800 (Accession NM_032840). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14800. Junctional Adhesion Molecule 1 (JAM1, Accession NM_144502) is another VGAM1382 host target gene. JAM1 BINDING SITE1 through JAM1 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by JAM1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM1 BINDING SITE1

through JAM1 BINDING SITE⁴, designated SEQ ID:29327, SEQ ID:29336, SEQ ID:29347 and SEQ ID:18860 respectively, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48506] Another function of VGAM1382 is therefore inhibition of Junctional Adhesion Molecule 1 (JAM1, Accession NM_144502). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM1. KIAA0275 (Accession NM_014767) is another VGAM1382 host target gene. KIAA0275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0275 BINDING SITE, designated SEQ ID:16549, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48507] Another function of VGAM1382 is therefore inhibition of KIAA0275 (Accession NM_014767). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0275. KIAA0494 (Accession NM_014774) is another VGAM1382 host target gene. KIAA0494 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0494 BINDING SITE, designated SEQ ID:16591, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48508] Another function of VGAM1382 is therefore inhibition of KIAA0494 (Accession NM_014774). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0494. KIAA1184 (Accession NM_022572) is another VGAM1382 host target gene. KIAA1184 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1184 BINDING SITE, designated SEQ ID:22896, to the

nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48509] Another function of VGAM1382 is therefore inhibition of KIAA1184 (Accession NM_022572). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1184. OBTP (Accession NM_017601) is another VGAM1382 host target gene. OBTP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OBTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBTP BINDING SITE, designated SEQ ID:19078, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48510] Another function of VGAM1382 is therefore inhibition of OBTP (Accession NM_017601). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBTP. RP4-622L5 (Accession NM_019118) is another VGAM1382 host target gene. RP4-622L5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by RP4-622L5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP4-622L5 BINDING SITE, designated SEQ ID:21203, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48511] Another function of VGAM1382 is therefore inhibition of RP4-622L5 (Accession NM_019118). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP4-622L5. LOC126302 (Accession XM_059020) is another VGAM1382 host target gene. LOC126302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126302 BINDING SITE, designated SEQ ID:36819, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48512] Another function of VGAM1382 is therefore inhibition of LOC126302 (Accession XM_059020). Accordingly, utilities

of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126302. LOC127602 (Accession XM_059166) is another VGAM1382 host target gene. LOC127602 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC127602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127602 BINDING SITE, designated SEQ ID:36905, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48513] Another function of VGAM1382 is therefore inhibition of LOC127602 (Accession XM_059166). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127602. LOC128954 (Accession XM_066252) is another VGAM1382 host target gene. LOC128954 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC128954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC128954 BINDING SITE, designated SEQ ID:37322, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48514] Another function of VGAM1382 is therefore inhibition of LOC128954 (Accession XM_066252). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128954. LOC136069 (Accession XM_069689) is another VGAM1382 host target gene. LOC136069 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC136069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC136069 BINDING SITE, designated SEQ ID:37390, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48515] Another function of VGAM1382 is therefore inhibition of LOC136069 (Accession XM_069689). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC136069. LOC148490 (Accession XM_086210) is another VGAM1382 host target gene. LOC148490 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148490 BINDING SITE, designated SEQ ID:38545, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48516] Another function of VGAM1382 is therefore inhibition of LOC148490 (Accession XM_086210). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148490. LOC149401 (Accession XM_086511) is another VGAM1382 host target gene. LOC149401 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149401 BINDING SITE, designated SEQ ID:38737, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48517] Another function of VGAM1382 is therefore inhibition of

LOC149401 (Accession XM_086511). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149401. LOC157273 (Accession XM_098743) is another VGAM1382 host target gene. LOC157273 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157273 BINDING SITE, designated SEQ ID:41785, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48518] Another function of VGAM1382 is therefore inhibition of LOC157273 (Accession XM_098743). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157273. LOC160156 (Accession XM_090047) is another VGAM1382 host target gene. LOC160156 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC160156 BINDING SITE, designated SEQ ID:39991, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48519] Another function of VGAM1382 is therefore inhibition of LOC160156 (Accession XM_090047). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160156. LOC161247 (Accession XM_090783) is another VGAM1382 host target gene. LOC161247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161247 BINDING SITE, designated SEQ ID:40015, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48520] Another function of VGAM1382 is therefore inhibition of LOC161247 (Accession XM_090783). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161247. LOC255779 (Accession XM_171147) is an-

other VGAM1382 host target gene. LOC255779 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255779, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255779 BINDING SITE, designated SEQ ID:45942, to the nucleotide sequence of VGAM1382 RNA, herein designated VGAM RNA, also designated SEQ ID:4093.

[48521] Another function of VGAM1382 is therefore inhibition of LOC255779 (Accession XM_171147). Accordingly, utilities of VGAM1382 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255779. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1383 (VGAM1383) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48522] VGAM1383 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1383 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[48523] VGAM1383 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus.

VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48524] VGAM1383 gene encodes a VGAM1383 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1383 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1383 precursor RNA is designated SEQ ID:1369, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1369 is located at position 7039 relative to the genome of Himetobi P Virus.

[48525] VGAM1383 precursor RNA folds onto itself, forming VGAM1383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48526] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1383 folded precursor RNA into VGAM1383 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1383 RNA is designated SEQ ID:4094, and is provided hereinbelow with reference to the sequence listing part.

[48527] VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1383 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48528] VGAM1383 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1383 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1383 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1383 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48529] The complementary binding of VGAM1383 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1383 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1383 host target RNA into VGAM1383 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48530] It is appreciated that VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1383 host target genes. The mRNA of each one of this plurality of VGAM1383 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1383 RNA, herein designated VGAM RNA, and which when bound by VGAM1383 RNA causes inhibition of translation of respective one or more VGAM1383 host target proteins.

[48531] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1383 gene, herein designated VGAM GENE, on one or more VGAM1383 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48532] It is yet further appreciated that a function of VGAM1383 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1383 correlate with, and may be deduced from, the identity of the host target genes which VGAM1383 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48533] Nucleotide sequences of the VGAM1383 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1383 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1383 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1383 are further described hereinbelow with reference to Table 1.

[48534] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1383 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1383 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48535] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1383 gene, herein designated VGAM is inhibition of expression of VGAM1383 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1383 correlate with, and may be deduced from, the identity of the target genes which VGAM1383 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48536] Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409) is a VGAM1383 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10662, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48537] A function of VGAM1383 is therefore inhibition of Dys-trophia Myotonica-protein Kinase (DMPK, Accession NM_004409). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. Claudin 15 (CLDN15, Accession NM_138429) is another VGAM1383 host target gene. CLDN15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLDN15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN15 BINDING SITE, designated SEQ ID:28792, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48538] Another function of VGAM1383 is therefore inhibition of Claudin 15 (CLDN15, Accession NM_138429). Accordingly, utilities of VGAM1383 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CLDN15. Hypermethylated In Cancer 2 (HIC2, Accession XM_036937) is another VGAM1383 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32532, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48539] Another function of VGAM1383 is therefore inhibition of Hypermethylated In Cancer 2 (HIC2, Accession XM_036937). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. KIAA1189 (Accession XM_050508) is another VGAM1383 host target gene. KIAA1189 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1189 BINDING SITE, designated SEQ

ID:35651, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48540] Another function of VGAM1383 is therefore inhibition of KIAA1189 (Accession XM_050508). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1189. KIAA1500 (Accession XM_034353) is another VGAM1383 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32062, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48541] Another function of VGAM1383 is therefore inhibition of KIAA1500 (Accession XM_034353). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. NIR3 (Accession XM_038799) is another VGAM1383 host target gene. NIR3 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by NIR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIR3 BINDING SITE, designated SEQ ID:32923, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48542] Another function of VGAM1383 is therefore inhibition of NIR3 (Accession XM_038799). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIR3. SPBPBP (Accession NM_006692) is another VGAM1383 host target gene. SPBPBP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SPBPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPBPBP BINDING SITE, designated SEQ ID:13508, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48543] Another function of VGAM1383 is therefore inhibition of

SPBPBP (Accession NM_006692). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPBPBP. Signal Transducer and Activator of Transcription 2, 113kDa (STAT2, Accession NM_005419) is another VGAM1383 host target gene. STAT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT2 BINDING SITE, designated SEQ ID:11890, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48544] Another function of VGAM1383 is therefore inhibition of Signal Transducer and Activator of Transcription 2, 113kDa (STAT2, Accession NM_005419). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT2. LOC119392 (Accession NM_145247) is another VGAM1383 host target gene. LOC119392 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC119392, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119392 BINDING SITE, designated SEQ ID:29757, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48545] Another function of VGAM1383 is therefore inhibition of LOC119392 (Accession NM_145247). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119392. LOC123242 (Accession XM_063548) is another VGAM1383 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37238, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48546] Another function of VGAM1383 is therefore inhibition of LOC123242 (Accession XM_063548). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC123242. LOC221688 (Accession XM_168085) is another VGAM1383 host target gene. LOC221688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221688 BINDING SITE, designated SEQ ID:44990, to the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48547] Another function of VGAM1383 is therefore inhibition of LOC221688 (Accession XM_168085). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221688. LOC253001 (Accession XM_171711) is another VGAM1383 host target gene. LOC253001 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46055, to

the nucleotide sequence of VGAM1383 RNA, herein designated VGAM RNA, also designated SEQ ID:4094.

[48548] Another function of VGAM1383 is therefore inhibition of LOC253001 (Accession XM_171711). Accordingly, utilities of VGAM1383 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253001. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1384 (VGAM1384) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48549] VGAM1384 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1384 was detected is described hereinabove with reference to Figs. 1–8.

[48550] VGAM1384 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus. VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48551] VGAM1384 gene encodes a VGAM1384 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1384 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1384 precursor RNA is designated SEQ ID:1370, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1370 is located at position 1905 relative to the genome of Himetobi P Virus.

[48552] VGAM1384 precursor RNA folds onto itself, forming VGAM1384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48553] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1384 folded precursor RNA into VGAM1384 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1384 RNA is designated SEQ ID:4095, and is provided hereinbelow with reference to the sequence listing part.

[48554] VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1384 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48555] VGAM1384 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1384 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1384 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48556] The complementary binding of VGAM1384 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1384 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1384 host target RNA into VGAM1384 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48557] It is appreciated that VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1384 host target genes. The mRNA of each one of this plurality of VGAM1384 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1384 RNA, herein designated VGAM RNA, and which when bound by VGAM1384 RNA causes inhibition of translation of respective one or more VGAM1384 host target proteins.

[48558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1384 gene, herein designated VGAM GENE, on one or more VGAM1384 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[48559] It is yet further appreciated that a function of VGAM1384 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1384 correlate with, and may be deduced from, the identity of the host target genes which VGAM1384 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48560] Nucleotide sequences of the VGAM1384 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1384 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1384 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1384 are further described hereinbelow with reference to Table 1.

[48561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1384 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1384 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48562] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1384 gene, herein designated VGAM is inhibition of expression of VGAM1384 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1384 correlate with, and may be deduced from, the identity of the target genes which VGAM1384 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48563] Homeo Box D3 (HOXD3, Accession NM_006898) is a VGAM1384 host target gene. HOXD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD3 BINDING SITE, designated SEQ ID:13775, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48564] A function of VGAM1384 is therefore inhibition of Homeo Box D3 (HOXD3, Accession NM_006898), a gene which

plays a role in the differentiation process of hematopoietic cells. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD3. The function of HOXD3 has been established by previous studies. Magli et al. (1991) presented evidence that the genomic organization of the human HOX genes reflects a regulatory hierarchy involved in the differentiation process of hematopoietic cells. Their results demonstrated that cells representing various stages of hematopoietic differentiation display differential patterns of HOX gene expression and that HOX genes are coordinately switched on or off in blocks that may include entire clusters. The entire HOX4 cluster was silent in all erythroleukemic, promyelocytic, and monocytic cell lines analyzed, and almost all the so-called HOX-2 genes (e.g., HOX2A; 142960; also symbolized HOXB5) were active in erythroleukemic cells and turned off in myeloid-restricted cells. Taniguchi et al. (1995) showed that overexpression of the HOX4A (HOXD3) gene in erythroleukemia cells resulted in increased levels of the GP IIb/IIIa complex (ITGA2B; 273800) and corresponding mRNA levels. The results implicated the HOXD3 gene in the regulation of cell adhesion processes. Animal model

experiments lend further support to the function of HOXD3. To examine directly the nature of functional overlap within the Hox3 family, Greer et al. (2000) exchanged reciprocally in the genome of mice the protein-coding portions of the Hoxa3 (OMIM Ref. No. 142954) and Hoxd3 genes. Thus, they generated mice that lacked any Hoxa3 protein but instead expressed the Hoxd3 protein from both the Hoxa3 and Hoxd3 loci, as well as mice that lacked Hoxd3 protein but expressed Hoxa3 from both loci. Embryos representing all Hoxa3 allelic combinations were examined histologically. At embryonic day 17.5, homozygous null Hoxa3 embryos demonstrated complete absence of the thymus. However, replacement of one or both copies of the Hoxa3 protein with the Hoxd3 protein restored this organ. Alterations of the hyoid cartilage, which is characteristic of embryos homozygous for the null allele of Hoxa3, were reversed by expression of the Hoxd3 protein at the Hoxa3 locus. One conclusion from this data was that the Hoxd3 protein is functionally equivalent to the Hoxa3 protein if it is expressed in the context of the Hoxa3 gene. A corollary would be that the Hoxa3 protein, if expressed at the Hoxd3 locus, would be unable to complement null mutations at Hoxa3. This was shown

to be the case. Hoxa3 protein was able to complement Hoxd3 deficiency when expressed in the context of the Hoxd3 allele. Greer et al. (2000) concluded that bidirectional complementation demonstrated that these proteins, which share less than 50% identity in the amino acid sequence, are capable of carrying out equivalent biologic functions in the processes recognized to require Hox3 gene activity. In addition, it provided direct evidence that the different roles played by these genes during embryogenesis are mainly the result of cis-acting sequences that modulate expression of the individual loci.

[48565] It is appreciated that the abovementioned animal model for HOXD3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[48566] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48567] Magli, M. C.; Barba, P.; Celetti, A.; De Vita, G.; Cillo, C.; Boncinelli, E. : Coordinate regulation of HOX genes in human hematopoietic cells. Proc. Nat. Acad. Sci. 88: 6348-6352, 1991. ; and

[48568] Taniguchi, Y.; Komatsu, N.; Moriuchi, T. : Overexpression

of the HOX4A (HOXD3) homeobox gene in human erythroleukemia HEL cells results in altered adhesive properties. Blood 85: 2786–279.

[48569] Further studies establishing the function and utilities of HOXD3 are found in John Hopkins OMIM database record ID 142980, and in cited publications numbered 5207, 318 and 5222–3187 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Jerky Homolog (mouse) (JRK, Accession XM_098818) is another VGAM1384 host target gene. JRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRK BINDING SITE, designated SEQ ID:41838, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48570] Another function of VGAM1384 is therefore inhibition of Jerky Homolog (mouse) (JRK, Accession XM_098818), a gene which might function as a DNA-binding protein. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with JRK. The function of JRK and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM210.3-oxoacid CoA Transferase (OXCT, Accession NM_000436) is another VGAM1384 host target gene. OXCT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OXCT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OXCT BINDING SITE, designated SEQ ID:6020, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48571] Another function of VGAM1384 is therefore inhibition of 3-oxoacid CoA Transferase (OXCT, Accession NM_000436). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OXCT. BH-protocadherin (brain-heart) (PCDH7, Accession NM_032456) is another VGAM1384 host target gene. PCDH7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH7, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH7 BINDING SITE, designated SEQ ID:26216, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48572] Another function of VGAM1384 is therefore inhibition of BH-protocadherin (brain-heart) (PCDH7, Accession NM_032456). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH7. Protein Kinase, AMP-activated, Beta 1 Non-catalytic Subunit (PRKAB1, Accession NM_006253) is another VGAM1384 host target gene. PRKAB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAB1 BINDING SITE, designated SEQ ID:12932, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48573] Another function of VGAM1384 is therefore inhibition of

Protein Kinase, AMP-activated, Beta 1 Non-catalytic Subunit (PRKAB1, Accession NM_006253), a gene which is responsible for the regulation of fatty acid synthesis by phosphorylation of acetyl-coa carboxylase. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAB1. The function of PRKAB1 has been established by previous studies. The mammalian 5-prime-AMP-activated protein kinase (AMPK) appears to act as a metabolic stress-sensing protein kinase. AMPK is a heterotrimeric protein composed of a catalytic alpha subunit, a noncatalytic beta subunit, and a noncatalytic gamma subunit. See PRKAA1 (OMIM Ref. No. 602739) for additional background. Using PCR with degenerate oligonucleotides based on the rat Ampk-beta-1 protein sequence, Woods et al. (1996) isolated rat liver cDNAs encoding Ampk-beta-1. Both the Ampk-beta-1 mRNA and protein are widely expressed in rat tissues. The predicted 270-amino acid protein has a calculated mass of 30 kD, but Woods et al. (1996) reported that it migrates as a 38-kD protein by SDS-PAGE. Immunoprecipitation studies suggested that Ampk-beta-1 mediates the association of the AMPK heterotrimeric complex in vitro. By searching

the sequence databases with a rat Ampk-beta-1 cDNA, Stapleton et al. (1997) identified an EST encoding human AMPK-beta-1. The human and rat AMPK-beta-1 proteins have 95% amino acid sequence identity. Thornton et al. (1998) reported that the predicted 271-amino acid human AMPK-beta-1 protein shares 71% sequence identity with human AMPK-beta-2 (PRKAB2; 602741). They found that both beta isoforms form complexes with Ampk-alpha-1 (OMIM Ref. No. PRKAA1) and Ampk-alpha-2 (PRKAA2; 600497) in rat liver and skeletal muscle. Coexpression of the alpha and AMPK-gamma-1 (PRKAG1; 602742) subunits with either AMPK-beta-1 or AMPK-beta-2 in mammalian cells did not reveal a significant difference in AMPK activity between the 2 beta isoforms. Using Western blot analysis and immunoprecipitation studies, Thornton et al. (1998) determined that Ampk-beta-1 was expressed at higher levels than Ampk-beta-2 in rat liver, while Ampk-beta-2 was more abundant in skeletal muscle. They suggested that the marked difference in expression patterns of Ampk-beta-1 and Ampk-beta-2 indicates tissue-specific roles for these isoforms. By Northern blot analysis, Thornton et al. (1998) found that AMPK-beta-1 was expressed as a 3-kb mRNA in all tissues tested. Stapleton

et al. (1997) mapped the human AMPK-beta-1 gene to 12q24.1 by fluorescence in situ hybridization

[48574] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48575] Stapleton, D.; Woollatt, E.; Mitchelhill, K. I.; Nicholl, J. K.; Fernandez, C. S.; Michell, B. J.; Witters, L. A.; Power, D. A.; Sutherland, G. R.; Kemp, B. E. : AMP-activated protein kinase isoenzyme family: subunit structure and chromosomal location. FEBS Lett. 409: 452-456, 1997. ; and

[48576] Thornton, C.; Snowden, M. A.; Carling, D. : Identification of a novel AMP-activated protein kinase beta subunit isoform that is highly expressed in skeletal muscle. J. Biol. Chem. 273: 1.

[48577] Further studies establishing the function and utilities of PRKAB1 are found in John Hopkins OMIM database record ID 602740, and in cited publications numbered 10696-5324 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prospero-related Homeobox 1 (PROX1, Accession NM_002763) is another VGAM1384 host target gene. PROX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

PROX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROX1 BINDING SITE, designated SEQ ID:8649, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48578] Another function of VGAM1384 is therefore inhibition of Prospero-related Homeobox 1 (PROX1, Accession NM_002763), a gene which may regulate gene expression and development of postmitotic undifferentiated young neurons. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROX1. The function of PROX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430.SMT3 Suppressor of Mif Two 3 Homolog 1 (yeast) (SMT3H1, Accession XM_009805) is another VGAM1384 host target gene. SMT3H1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMT3H1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SMT3H1 BINDING SITE, designated SEQ ID:30128, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48579] Another function of VGAM1384 is therefore inhibition of SMT3 Suppressor of Mif Two 3 Homolog 1 (yeast) (SMT3H1, Accession XM_009805), a gene which is involved in the function and/or structure of the eukaryotic kinetochore. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMT3H1. The function of SMT3H1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM119. Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM_003304) is another VGAM1384 host target gene. TRPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC1 BIND-

ING SITE, designated SEQ ID:9309, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48580] Another function of VGAM1384 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM_003304), a gene which acts as a non-voltage-sensitive store-operated Ca^{2+} channel. Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC1. The function of TRPC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM_001732) is another VGAM1384 host target gene. BTN1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN1A1 BINDING SITE, designated SEQ ID:7468, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ

ID:4095.

[48581] Another function of VGAM1384 is therefore inhibition of Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM_001732). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN1A1. CRA (Accession NM_006697) is another VGAM1384 host target gene. CRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRA BINDING SITE, designated SEQ ID:13517, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48582] Another function of VGAM1384 is therefore inhibition of CRA (Accession NM_006697). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRA. DKFZP434A043 (Accession NM_015396) is another VGAM1384 host target gene. DKFZP434A043 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434A043,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434A043 BINDING SITE, designated SEQ ID:17706, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48583] Another function of VGAM1384 is therefore inhibition of DKFZP434A043 (Accession NM_015396). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434A043. FLJ10853 (Accession NM_018246) is another VGAM1384 host target gene. FLJ10853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated SEQ ID:20215, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48584] Another function of VGAM1384 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of

VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. FLJ23462 (Accession NM_024843) is another VGAM1384 host target gene. FLJ23462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23462 BINDING SITE, designated SEQ ID:24269, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48585] Another function of VGAM1384 is therefore inhibition of FLJ23462 (Accession NM_024843). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23462. HSPC019 (Accession NM_014028) is another VGAM1384 host target gene. HSPC019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC019

BINDING SITE, designated SEQ ID:15253, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48586] Another function of VGAM1384 is therefore inhibition of HSPC019 (Accession NM_014028). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC019. KIAA0057 (Accession NM_012288) is another VGAM1384 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14625, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48587] Another function of VGAM1384 is therefore inhibition of KIAA0057 (Accession NM_012288). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA0429 (Accession NM_014751) is another VGAM1384 host target gene. KIAA0429 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16474, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48588] Another function of VGAM1384 is therefore inhibition of KIAA0429 (Accession NM_014751). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. KIAA0523 (Accession XM_041964) is another VGAM1384 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33641, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48589] Another function of VGAM1384 is therefore inhibition of

KIAA0523 (Accession XM_041964). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. KIAA1538 (Accession XM_049474) is another VGAM1384 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35436, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48590] Another function of VGAM1384 is therefore inhibition of KIAA1538 (Accession XM_049474). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. KIAA1644 (Accession XM_097892) is another VGAM1384 host target gene. KIAA1644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1644 BINDING SITE, designated SEQ ID:41202, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48591] Another function of VGAM1384 is therefore inhibition of KIAA1644 (Accession XM_097892). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1644. S164 (Accession XM_027330) is another VGAM1384 host target gene. S164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by S164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of S164 BINDING SITE, designated SEQ ID:30484, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48592] Another function of VGAM1384 is therefore inhibition of S164 (Accession XM_027330). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with S164. Serine/threonine Kinase 33 (STK33, Accession

XM_031831) is another VGAM1384 host target gene.

STK33 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by STK33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK33 BINDING SITE, designated SEQ ID:31496, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48593] Another function of VGAM1384 is therefore inhibition of Serine/threonine Kinase 33 (STK33, Accession XM_031831). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK33. LOC118611 (Accession XM_061055) is another VGAM1384 host target gene. LOC118611 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC118611, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118611 BINDING SITE, designated SEQ ID:37186, to the nucleotide sequence of

VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48594] Another function of VGAM1384 is therefore inhibition of LOC118611 (Accession XM_061055). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118611. LOC124044 (Accession XM_071871) is another VGAM1384 host target gene. LOC124044 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124044, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124044 BINDING SITE, designated SEQ ID:37434, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48595] Another function of VGAM1384 is therefore inhibition of LOC124044 (Accession XM_071871). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124044. LOC144110 (Accession XM_084735) is another VGAM1384 host target gene. LOC144110 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC144110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144110 BINDING SITE, designated SEQ ID:37678, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48596] Another function of VGAM1384 is therefore inhibition of LOC144110 (Accession XM_084735). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144110. LOC149832 (Accession XM_097733) is another VGAM1384 host target gene. LOC149832 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149832 BINDING SITE, designated SEQ ID:41080, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48597] Another function of VGAM1384 is therefore inhibition of LOC149832 (Accession XM_097733). Accordingly, utilities

of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149832. LOC155038 (Accession XM_088130) is another VGAM1384 host target gene. LOC155038 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155038, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155038 BINDING SITE, designated SEQ ID:39534, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48598] Another function of VGAM1384 is therefore inhibition of LOC155038 (Accession XM_088130). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155038. LOC220020 (Accession XM_167821) is another VGAM1384 host target gene. LOC220020 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220020 BINDING SITE, designated SEQ ID:44868, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48599] Another function of VGAM1384 is therefore inhibition of LOC220020 (Accession XM_167821). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220020. LOC253842 (Accession XM_173230) is another VGAM1384 host target gene. LOC253842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253842 BINDING SITE, designated SEQ ID:46505, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48600] Another function of VGAM1384 is therefore inhibition of LOC253842 (Accession XM_173230). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253842. LOC255475 (Accession XM_174861) is another VGAM1384 host target gene. LOC255475 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255475 BINDING SITE, designated SEQ ID:46605, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48601] Another function of VGAM1384 is therefore inhibition of LOC255475 (Accession XM_174861). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255475. LOC91263 (Accession XM_037264) is another VGAM1384 host target gene. LOC91263 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91263 BINDING SITE, designated SEQ ID:32595, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48602] Another function of VGAM1384 is therefore inhibition of

LOC91263 (Accession XM_037264). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91263. LOC91818 (Accession XM_040878) is another VGAM1384 host target gene. LOC91818 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91818 BINDING SITE, designated SEQ ID:33406, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48603] Another function of VGAM1384 is therefore inhibition of LOC91818 (Accession XM_040878). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91818. LOC91923 (Accession XM_041526) is another VGAM1384 host target gene. LOC91923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC91923 BINDING SITE, designated SEQ ID:33546, to the nucleotide sequence of VGAM1384 RNA, herein designated VGAM RNA, also designated SEQ ID:4095.

[48604] Another function of VGAM1384 is therefore inhibition of LOC91923 (Accession XM_041526). Accordingly, utilities of VGAM1384 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91923. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1385 (VGAM1385) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48605] VGAM1385 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1385 was detected is described hereinabove with reference to Figs. 1–8.

[48606] VGAM1385 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus. VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[48607] VGAM1385 gene encodes a VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1385 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1385 precursor RNA is designated SEQ ID:1371, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1371 is located at position 2435 relative to the genome of Himetobi P Virus.

[48608] VGAM1385 precursor RNA folds onto itself, forming VGAM1385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48609] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1385 folded precursor RNA into VGAM1385 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1385 RNA is designated SEQ ID:4096, and is provided hereinbelow with reference to the sequence listing part.

[48610] VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1385 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48611] VGAM1385 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1385 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1385 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48612] The complementary binding of VGAM1385 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1385 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1385 host target RNA into VGAM1385 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48613] It is appreciated that VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1385 host target genes. The mRNA of each one of this plurality of VGAM1385 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1385 RNA, herein designated VGAM RNA, and which when bound by VGAM1385 RNA causes inhibition of translation of respective one or more VGAM1385 host target proteins.

[48614] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1385 gene, herein designated VGAM GENE, on one or more VGAM1385 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48615] It is yet further appreciated that a function of VGAM1385 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1385 correlate with, and may be deduced from, the identity of the host target genes which VGAM1385 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48616] Nucleotide sequences of the VGAM1385 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1385 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1385 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1385 are further described hereinbelow with reference to Table 1.

[48617] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1385 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1385 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48618] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1385 gene, herein designated VGAM is inhibition of expression of VGAM1385 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1385 correlate with, and may be deduced from, the identity of the target genes which VGAM1385 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48619] Adenosine A1 Receptor (ADORA1, Accession NM_000674) is a VGAM1385 host target gene. ADORA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADORA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADORA1 BINDING SITE, designated SEQ ID:6328, to the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, also designated SEQ ID:4096.

[48620] A function of VGAM1385 is therefore inhibition of Adenosine A1 Receptor (ADORA1, Accession NM_000674), a gene which the activity of this receptor is mediated by G proteins which inhibit adenylyl cyclase. Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADORA1. The function of ADORA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM234. Anaplastic Lymphoma Kinase (Ki-1) (ALK, Accession XM_055726) is another VGAM1385 host target gene. ALK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ALK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALK BINDING SITE, designated SEQ ID:36321, to the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, also designated SEQ ID:4096.

[48621] Another function of VGAM1385 is therefore inhibition of Anaplastic Lymphoma Kinase (Ki-1) (ALK, Accession XM_055726). Accordingly, utilities of VGAM1385 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with ALK. Frequently Rearranged In Advanced T-cell Lymphomas 2 (FRAT2, Accession NM_012083) is another VGAM1385 host target gene. FRAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FRAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRAT2 BINDING SITE, designated SEQ ID:14372, to the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, also designated SEQ ID:4096.

[48622] Another function of VGAM1385 is therefore inhibition of Frequently Rearranged In Advanced T-cell Lymphomas 2 (FRAT2, Accession NM_012083), a gene which binds gsk-3 and prevents gsk-3-dependent phosphorylation. Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FRAT2. The function of FRAT2 has been established by previous studies. Dorsal accumulation of beta-catenin (CTNNB1; 116806) in early *Xenopus* embryos is required for body axis formation. Beta-catenin is dor-

sally stabilized by the localized inhibition of the kinase GSK3 (see OMIM Ref. No. GSK3B; 605004). Using a yeast 2-hybrid system to identify a cytoplasmic regulator of Xenopus GSK3, Yost et al. (1998) isolated an oocyte cDNA encoding a 169-amino acid protein that they termed GSK3-binding protein, or GBP. By searching sequence databases, Yost et al. (1998) identified 2 homologous human sequences, FRAT1 (OMIM Ref. No. 602503) and FRAT2, a partial sequence that shares 59% amino acid identity with FRAT1. Sequence analysis predicted that GBP and the FRAT proteins contain 3 well-conserved regions. Binding and functional analyses revealed that the GSK3-binding and -inhibitory activities of GBP and FRAT2 reside in the C-terminal conserved domain III sequence. The authors proposed that GBP, FRAT1, and FRAT2 form a family of GSK3-binding proteins that inhibit the phosphorylation of beta-catenin, preventing its degradation by the ubiquitin-proteasome pathway. By screening a fetal lung cDNA library with an FT2S probe, which was obtained from a gastric cancer cell line, that corresponds to an FRAT2 EST, Saitoh et al. (2001) isolated a full-length cDNA encoding FRAT2. The deduced 233-amino acid protein, which is 77% identical to FRAT1, contains an N-

terminal acidic domain followed by a proline-rich domain and a GSK3B-binding domain near the C terminus, which is highly divergent from that of FRAT1. Northern blot analysis detected a 2.4-kb transcript, with highest expression in pancreas, heart, spleen, placenta, skeletal muscle, liver, peripheral blood leukocytes, and fetal kidney. Expression was higher in gastric cancer, cervical cancer, and chronic myelogenous leukemia cell lines than in other cancer cell lines. Functional analysis in the *Xenopus* axis duplication assay indicated that FRAT2 is a positive regulator of the WNT (see OMIM Ref. No. 164975) signaling pathway. Saitoh et al. (2001) suggested that upregulation of FRAT2 in human cancer may be implicated in carcinogenesis through activation of the WNT signaling pathway.

[48623] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48624] Saitoh, T.; Moriwaki, J.; Koike, J.; Takagi, A.; Miwa, T.; Shiokawa, K.; Katoh, M. : Molecular cloning and characterization of FRAT2, encoding a positive regulator of the WNT signaling pathway. *Biochem. Biophys. Res. Commun.* 281: 815–820, 2001. ; and

[48625] Yost, C.; Farr, G. H., III; Pierce, S. B.; Ferkey, D. M.; Chen, M. M.; Kimelman, D. : GBP, an inhibitor of GSK-3, is implicated in *Xenopus* development and oncogenesis. *Cell* 93: 1031-10.

[48626] Further studies establishing the function and utilities of FRAT2 are found in John Hopkins OMIM database record ID 605006, and in cited publications numbered 291 and 9026 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10726 (Accession NM_018195) is another VGAM1385 host target gene. FLJ10726 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10726 BINDING SITE, designated SEQ ID:20056, to the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, also designated SEQ ID:4096.

[48627] Another function of VGAM1385 is therefore inhibition of FLJ10726 (Accession NM_018195). Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ10726. LOC219848 (Accession XM_166170) is another VGAM1385 host target gene. LOC219848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219848 BINDING SITE, designated SEQ ID:43987, to the nucleotide sequence of VGAM1385 RNA, herein designated VGAM RNA, also designated SEQ ID:4096.

[48628] Another function of VGAM1385 is therefore inhibition of LOC219848 (Accession XM_166170). Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219848. LOC255031 (Accession XM_173187) is another VGAM1385 host target gene. LOC255031 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255031 BINDING SITE, designated SEQ ID:46432, to the nucleotide sequence of VGAM1385 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4096.

[48629] Another function of VGAM1385 is therefore inhibition of LOC255031 (Accession XM_173187). Accordingly, utilities of VGAM1385 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255031. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1386 (VGAM1386) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48630] VGAM1386 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1386 was detected is described hereinabove with reference to Figs. 1–8.

[48631] VGAM1386 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Himetobi P Virus. VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48632] VGAM1386 gene encodes a VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1386 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1386 precursor RNA is designated SEQ ID:1372, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1372 is located at position 8878 relative to the genome of Himetobi P Virus.

- [48633] VGAM1386 precursor RNA folds onto itself, forming VGAM1386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48634] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1386 folded precursor RNA into VGAM1386 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM1386 RNA is designated SEQ ID:4097, and is provided hereinbelow with reference to the sequence listing part.

[48635] VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1386 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48636] VGAM1386 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1386 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1386 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48637] The complementary binding of VGAM1386 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1386 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1386 host target RNA into VGAM1386 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48638] It is appreciated that VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1386 host target genes. The mRNA of

each one of this plurality of VGAM1386 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1386 RNA, herein designated VGAM RNA, and which when bound by VGAM1386 RNA causes inhibition of translation of respective one or more VGAM1386 host target proteins.

[48639] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1386 gene, herein designated VGAM GENE, on one or more VGAM1386 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[48640] It is yet further appreciated that a function of VGAM1386 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1386 correlate with, and may be deduced from, the identity of the host target genes which VGAM1386 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48641] Nucleotide sequences of the VGAM1386 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1386 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1386 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1386 are further described hereinbelow with reference to Table 1.

[48642] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1386 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1386 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48643] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1386 gene, herein designated VGAM is inhibition of expression of VGAM1386 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1386 correlate with, and may be deduced from, the identity of the target genes which VGAM1386 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48644] ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028) is a VGAM1386 host target gene. ATP11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11A BINDING SITE, designated SEQ ID:37803, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48645] A function of VGAM1386 is therefore inhibition of ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028). Accordingly, utilities of VGAM1386 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with ATP11A. Integrin, Alpha M (complement component receptor 3, alpha; also known as CD11b (p170), Macrophage Antigen Alpha Polypeptide) (ITGAM, Accession NM_000632) is another VGAM1386 host target gene. ITGAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGAM BINDING SITE, designated SEQ ID:6247, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48646] Another function of VGAM1386 is therefore inhibition of Integrin, Alpha M (complement component receptor 3, alpha; also known as CD11b (p170), Macrophage Antigen Alpha Polypeptide) (ITGAM, Accession NM_000632), a gene which is involved in various adhesive interactions of monocytes, macrophages and granulocytes as well as in mediating the uptake of complement-coated particles. Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with ITGAM. The function of ITGAM has been established by previous studies. A major surface antigen family on human leukocytes includes complement receptor type 3 (CR3A; also called integrin alpha-M, Mac1 or Mo1), lymphocyte function-associated antigen type 1 (LFA-1; 153370), and p150,95 (Leu M5; 151510). These antigens share a common beta chain (OMIM Ref. No. 116920) of 94 kD, linked noncovalently to 1 of 3 alpha chains distinctive to each. They promote adhesion of granulocytes to each other and to endothelial cell monolayers. The apparent molecular weight of the Mo1 alpha chain is 155 to 165 kD, that of the LFA1 alpha subunit is 180 kD, and that of the Leu M5 subunit is 130 to 150 kD. Pierce et al. (1986) purified human Mo1 to homogeneity from normal granulocytes by affinity chromatography and high performance liquid chromatography (HPLC) and determined the N-terminal amino acid sequence of its alpha subunit. The obtained sequence was identical, except for 2 conservative substitutions, to that of the alpha subunit of Mac1 antigen (Springer et al., 1985). Furthermore, Pierce et al. (1986) found that the N-terminal amino acid sequence of the alpha subunit of Mo1 was homologous to the alpha subunit of IIb/IIIa, a glycoprotein that serves

similar adhesive functions on platelets and is deficient or defective in Glanzmann thrombasthenia (OMIM Ref. No. 273800). Patients with a history of recurrent bacterial infections and an inherited deficiency of all 3 leukocyte membrane surface antigens are thought to have reduced or absent synthesis of the common beta subunit of the antigen family; see 116920. By Southern analysis of DNA from hamster-human hybrids, Arnaout et al. (1988) localized the human MO1A gene to chromosome 16, which has been shown to contain the gene LFA1A (OMIM Ref. No. 153370). By in situ hybridization, Corbi et al. (1988) demonstrated that the alpha subunits of LFA-1, Mac1, and p150,95 constitute a cluster that might be called leukocyte adhesion, alpha, cluster (LAAC) located on 16p13.1-p11. Callen et al. (1991) narrowed the assignment to 16p11.2. Inflammation plays an essential role in the initiation and progression of atherosclerosis. Simon et al. (2000) presented evidence that it also has a role in vascular repair after mechanical arterial injury (i.e., percutaneous transluminal coronary angioplasty, or PTCA). In animal models of vascular injury, leukocytes are recruited as a precursor to intimal thickening. Markers of leukocyte activation, in particular, increased expression of Mac1,

which is responsible for firm leukocyte adhesion to platelets and fibrinogen on denuded vessels, predict restenosis after PTCA. To determine whether Mac1-mediated leukocyte recruitment is causally related to neointimal formation, Simon et al. (2000) subjected Mac1 knockout mice to a mechanical carotid artery dilation and complete endothelial denudation. They found that the selective absence of Mac1 impaired transplatelet leukocyte migration into the vessel wall, reducing leukocyte accumulation. Diminished medial leukocyte accumulation was accompanied by markedly reduced neointimal thickening after vascular injury. These data established a role for inflammation in neointimal thickening and suggested that leukocyte recruitment to mechanically injured arteries may prevent restenosis

[48647] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48648] Pierce, M. W.; Remold-O'Donnell, E.; Todd, R. F., III; Arnaout, M. A. : N-terminal sequence of human leukocyte glycoprotein Mo1: conservation across species and homology to platelet IIb/IIIa. *Biochim. Biophys. Acta* 874: 368-371, 1986. ; and

[48649] Arnaout, M. A.; Remold-O'Donnell, E.; Pierce, M. W.; Harris, P.; Tenen, D. G. : Molecular cloning of the alpha-subunit of human and guinea pig leukocyte adhesion glycoprotein Mo1: chromo.

[48650] Further studies establishing the function and utilities of ITGAM are found in John Hopkins OMIM database record ID 120980, and in cited publications numbered 4960–4967 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CSR1 (Accession NM_016240) is another VGAM1386 host target gene. CSR1 BINDING SITE1 and CSR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CSR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSR1 BINDING SITE1 and CSR1 BINDING SITE2, designated SEQ ID:18357 and SEQ ID:18358 respectively, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48651] Another function of VGAM1386 is therefore inhibition of CSR1 (Accession NM_016240). Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CSR1. FLJ11618 (Accession NM_022452) is another VGAM1386 host target gene. FLJ11618 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11618 BINDING SITE, designated SEQ ID:22792, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48652] Another function of VGAM1386 is therefore inhibition of FLJ11618 (Accession NM_022452). Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11618. KIAA0914 (Accession NM_014883) is another VGAM1386 host target gene. KIAA0914 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0914, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0914 BINDING SITE, designated SEQ ID:17036, to the

nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48653] Another function of VGAM1386 is therefore inhibition of KIAA0914 (Accession NM_014883). Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0914. MGC20255 (Accession NM_052848) is another VGAM1386 host target gene. MGC20255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20255 BINDING SITE, designated SEQ ID:27427, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48654] Another function of VGAM1386 is therefore inhibition of MGC20255 (Accession NM_052848). Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20255. LOC162461 (Accession XM_091568) is another VGAM1386 host target gene. LOC162461 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC162461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162461 BINDING SITE, designated SEQ ID:40057, to the nucleotide sequence of VGAM1386 RNA, herein designated VGAM RNA, also designated SEQ ID:4097.

[48655] Another function of VGAM1386 is therefore inhibition of LOC162461 (Accession XM_091568). Accordingly, utilities of VGAM1386 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162461. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1387 (VGAM1387) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48656] VGAM1387 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1387 was detected is described hereinabove with reference to Figs. 1-8.

[48657] VGAM1387 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Himetobi P Virus.

VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48658] VGAM1387 gene encodes a VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1387 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1387 precursor RNA is designated SEQ ID:1373, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1373 is located at position 7593 relative to the genome of Himetobi P Virus.

[48659] VGAM1387 precursor RNA folds onto itself, forming VGAM1387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48660] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1387 folded precursor RNA into VGAM1387 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1387 RNA is designated SEQ ID:4098, and is provided hereinbelow with reference to the sequence listing part.

[48661] VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1387 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48662] VGAM1387 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1387 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1387 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48663] The complementary binding of VGAM1387 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1387 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1387

host target RNA into VGAM1387 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48664] It is appreciated that VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1387 host target genes. The mRNA of each one of this plurality of VGAM1387 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1387 RNA, herein designated VGAM RNA, and which when bound by VGAM1387 RNA causes inhibition of translation of respective one or more VGAM1387 host target proteins.

[48665] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1387 gene, herein designated VGAM GENE, on one or more VGAM1387 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48666] It is yet further appreciated that a function of VGAM1387 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGAM1387 correlate with, and may be deduced from, the identity of the host target genes which VGAM1387 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48667] Nucleotide sequences of the VGAM1387 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1387 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1387 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1387 are further

described hereinbelow with reference to Table 1.

[48668] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1387 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1387 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48669] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1387 gene, herein designated VGAM is inhibition of expression of VGAM1387 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1387 correlate with, and may be deduced from, the identity of the target genes which VGAM1387 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48670] B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898) is a VGAM1387 host target gene. BCL11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of BCL11B BINDING SITE, designated SEQ ID:23169, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48671] A function of VGAM1387 is therefore inhibition of B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11B. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063) is another VGAM1387 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11493, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48672] Another function of VGAM1387 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of

VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM314. Transcription Factor-like 4 (TCFL4, Accession XM_032817) is another VGAM1387 host target gene. TCFL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCFL4 BINDING SITE, designated SEQ ID:31768, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48673] Another function of VGAM1387 is therefore inhibition of Transcription Factor-like 4 (TCFL4, Accession XM_032817), a gene which interacts with Mad and represses transcription by recruiting the Sin3A-histone deacetylase corepressor complex. Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL4.

The function of TCFL4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM_003392) is another VGAM1387 host target gene. WNT5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WNT5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT5A BINDING SITE, designated SEQ ID:9430, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48674] Another function of VGAM1387 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 5A (WNT5A, Accession NM_003392), a gene which is a ligand for members of the frizzled family of seven transmembrane receptors and is probably a developmental protein. Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT5A. The function of WNT5A and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM996. Zinc Finger Protein 161 (ZNF161, Accession NM_007146) is another VGAM1387 host target gene. ZNF161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF161 BINDING SITE, designated SEQ ID:13997, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48675] Another function of VGAM1387 is therefore inhibition of Zinc Finger Protein 161 (ZNF161, Accession NM_007146). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF161. Basic Leucine Zipper and W2 Domains 1 (BZW1, Accession NM_014670) is another VGAM1387 host target gene. BZW1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BZW1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of BZW1 BINDING SITE, designated SEQ ID:16128, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48676] Another function of VGAM1387 is therefore inhibition of Basic Leucine Zipper and W2 Domains 1 (BZW1, Accession NM_014670). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BZW1. Cysteine and Histidine-rich Domain (CHORD)-containing, Zinc Binding Protein 1 (CHORDC1, Accession NM_012124) is another VGAM1387 host target gene. CHORDC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHORDC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHORDC1 BINDING SITE, designated SEQ ID:14436, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48677] Another function of VGAM1387 is therefore inhibition of Cysteine and Histidine-rich Domain (CHORD)-containing, Zinc Binding Protein 1 (CHORDC1, Accession NM_012124).

Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHORDC1. DKFZP434A043 (Accession NM_015396) is another VGAM1387 host target gene. DKFZP434A043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434A043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434A043 BINDING SITE, designated SEQ ID:17699, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48678] Another function of VGAM1387 is therefore inhibition of DKFZP434A043 (Accession NM_015396). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434A043. DKFZP434L0718 (Accession NM_032139) is another VGAM1387 host target gene. DKFZP434L0718 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434L0718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L0718 BINDING SITE, designated SEQ ID:25821, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48679] Another function of VGAM1387 is therefore inhibition of DKFZP434L0718 (Accession NM_032139). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L0718. FLJ11827 (Accession NM_025093) is another VGAM1387 host target gene. FLJ11827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11827 BINDING SITE, designated SEQ ID:24721, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48680] Another function of VGAM1387 is therefore inhibition of FLJ11827 (Accession NM_025093). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ11827. FLJ22944 (Accession NM_025145) is another VGAM1387 host target gene. FLJ22944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22944 BINDING SITE, designated SEQ ID:24781, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48681] Another function of VGAM1387 is therefore inhibition of FLJ22944 (Accession NM_025145). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22944. KIAA1371 (Accession XM_114371) is another VGAM1387 host target gene. KIAA1371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1371 BINDING SITE, designated SEQ ID:42908, to the nucleotide sequence of VGAM1387 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4098.

[48682] Another function of VGAM1387 is therefore inhibition of KIAA1371 (Accession XM_114371). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1371. KIAA1755 (Accession XM_028810) is another VGAM1387 host target gene. KIAA1755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1755 BINDING SITE, designated SEQ ID:30747, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48683] Another function of VGAM1387 is therefore inhibition of KIAA1755 (Accession XM_028810). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1755. KIAA1795 (Accession XM_050988) is another VGAM1387 host target gene. KIAA1795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1795, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1795 BINDING SITE, designated SEQ ID:35699, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48684] Another function of VGAM1387 is therefore inhibition of KIAA1795 (Accession XM_050988). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1795. RNAHP (Accession NM_007372) is another VGAM1387 host target gene. RNAHP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNAHP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAHP BINDING SITE, designated SEQ ID:14299, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48685] Another function of VGAM1387 is therefore inhibition of RNAHP (Accession NM_007372). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with RNAHP. Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832) is another VGAM1387 host target gene. SLC26A7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC26A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A7 BINDING SITE, designated SEQ ID:27411, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48686] Another function of VGAM1387 is therefore inhibition of Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A7. Zinc Finger, DHHC Domain Containing 5 (ZDHHC5, Accession XM_166204) is another VGAM1387 host target gene. ZDHHC5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZDHHC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of ZDHHC5 BINDING SITE, designated SEQ ID:44008, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48687] Another function of VGAM1387 is therefore inhibition of Zinc Finger, DHHC Domain Containing 5 (ZDHHC5, Accession XM_166204). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC5. LOC145098 (Accession XM_085022) is another VGAM1387 host target gene. LOC145098 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145098 BINDING SITE, designated SEQ ID:37795, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48688] Another function of VGAM1387 is therefore inhibition of LOC145098 (Accession XM_085022). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145098. LOC146795 (Accession XM_085593) is another VGAM1387 host target gene. LOC146795 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146795 BINDING SITE, designated SEQ ID:38242, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48689] Another function of VGAM1387 is therefore inhibition of LOC146795 (Accession XM_085593). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146795. LOC148266 (Accession XM_086128) is another VGAM1387 host target gene. LOC148266 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148266 BINDING SITE, designated SEQ ID:38514, to

the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48690] Another function of VGAM1387 is therefore inhibition of LOC148266 (Accession XM_086128). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148266. LOC151579 (Accession XM_045290) is another VGAM1387 host target gene. LOC151579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151579 BINDING SITE, designated SEQ ID:34422, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48691] Another function of VGAM1387 is therefore inhibition of LOC151579 (Accession XM_045290). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151579. LOC152620 (Accession XM_011108) is another VGAM1387 host target gene. LOC152620 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC152620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152620 BINDING SITE, designated SEQ ID:30174, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48692] Another function of VGAM1387 is therefore inhibition of LOC152620 (Accession XM_011108). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152620. LOC199907 (Accession XM_114051) is another VGAM1387 host target gene. LOC199907 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199907, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199907 BINDING SITE, designated SEQ ID:42657, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48693] Another function of VGAM1387 is therefore inhibition of LOC199907 (Accession XM_114051). Accordingly, utilities

of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199907. LOC255565 (Accession XM_170811) is another VGAM1387 host target gene. LOC255565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255565 BINDING SITE, designated SEQ ID:45591, to the nucleotide sequence of VGAM1387 RNA, herein designated VGAM RNA, also designated SEQ ID:4098.

[48694] Another function of VGAM1387 is therefore inhibition of LOC255565 (Accession XM_170811). Accordingly, utilities of VGAM1387 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255565. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1388 (VGAM1388) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48695] VGAM1388 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1388 was detected is described hereinabove with reference to Figs. 1–8.

[48696] VGAM1388 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48697] VGAM1388 gene encodes a VGAM1388 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1388 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1388 precursor RNA is designated SEQ ID:1374, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1374 is located at position 58541 relative to the genome of Cercopithecine Herpesvirus 7.

[48698] VGAM1388 precursor RNA folds onto itself, forming VGAM1388 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48699] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1388 folded precursor RNA into VGAM1388 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1388 RNA is designated SEQ ID:4099, and is provided hereinbelow with reference to the sequence listing part.

[48700] VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1388 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[48701] VGAM1388 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1388 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1388 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48702] The complementary binding of VGAM1388 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1388 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1388 host target RNA into VGAM1388 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48703] It is appreciated that VGAM1388 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1388 host target genes. The mRNA of each one of this plurality of VGAM1388 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1388 RNA, herein designated VGAM RNA, and which when bound by VGAM1388 RNA causes inhibition of translation of respective one or more VGAM1388 host target proteins.

[48704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1388 gene, herein designated VGAM GENE, on one or more VGAM1388 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48705] It is yet further appreciated that a function of VGAM1388 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1388 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1388 correlate with, and may be deduced from, the identity of the host target genes which VGAM1388 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48706] Nucleotide sequences of the VGAM1388 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1388 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1388 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1388 are further
described hereinbelow with reference to Table 1.

[48707] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1388 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1388 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[48708] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1388 gene, herein designated VGAM is
inhibition of expression of VGAM1388 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1388 correlate with, and may be deduced
from, the identity of the target genes which VGAM1388
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[48709] DXS1283E (Accession XM_047871) is a VGAM1388 host
target gene. DXS1283E BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by DXS1283E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DXS1283E BINDING SITE, designated SEQ ID:35060, to the nucleotide sequence of VGAM1388 RNA, herein designated VGAM RNA, also designated SEQ ID:4099.

[48710] A function of VGAM1388 is therefore inhibition of DXS1283E (Accession XM_047871). Accordingly, utilities of VGAM1388 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DXS1283E. TOPBP1 (Accession NM_007027) is another VGAM1388 host target gene. TOPBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOPBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOPBP1 BINDING SITE, designated SEQ ID:13885, to the nucleotide sequence of VGAM1388 RNA, herein designated VGAM RNA, also designated SEQ ID:4099.

[48711] Another function of VGAM1388 is therefore inhibition of

TOPBP1 (Accession NM_007027). Accordingly, utilities of VGAM1388 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOPBP1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1389 (VGAM1389) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48712] VGAM1389 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1389 was detected is described hereinabove with reference to Figs. 1-8.

[48713] VGAM1389 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48714] VGAM1389 gene encodes a VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1389 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1389 precursor RNA is designated SEQ ID:1375, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1375 is located at position 56184 relative to the genome of Cercopithecine Herpesvirus 7.

- [48715] VGAM1389 precursor RNA folds onto itself, forming VGAM1389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48716] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1389 folded precursor RNA into VGAM1389 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide se-

quence of VGAM1389 RNA is designated SEQ ID:4100, and is provided hereinbelow with reference to the sequence listing part.

[48717] VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1389 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48718] VGAM1389 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1389 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1389 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48719] The complementary binding of VGAM1389 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1389 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1389 host target RNA into VGAM1389 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48720] It is appreciated that VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1389 host target genes. The mRNA of each one of this plurality of VGAM1389 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1389 RNA, herein designated VGAM RNA, and which when bound by VGAM1389 RNA causes inhibition of translation of respective one or more VGAM1389 host target proteins.

[48721] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1389 gene, herein designated VGAM GENE, on one or more VGAM1389 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48722] It is yet further appreciated that a function of VGAM1389

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1389 correlate with, and may be deduced from, the identity of the host target genes which VGAM1389 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48723] Nucleotide sequences of the VGAM1389 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1389 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1389 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1389 are further described hereinbelow with reference to Table 1.

[48724] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1389 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1389 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48725] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1389 gene, herein designated VGAM is inhibition of expression of VGAM1389 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1389 correlate with, and may be deduced from, the identity of the target genes which VGAM1389 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48726] Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052) is a VGAM1389 host target gene. DSCR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR3 BINDING SITE, designated SEQ ID:12683, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48727] A function of VGAM1389 is therefore inhibition of Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR3. Mannosyl

(alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410) is another VGAM1389 host target gene. MGAT5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT5 BINDING SITE, designated SEQ ID:8236, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48728] Another function of VGAM1389 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT5. Phosphoinositide-3-kinase, Catalytic, Gamma Polypeptide (PIK3CG, Accession NM_002649) is another VGAM1389 host target gene. PIK3CG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PIK3CG, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3CG BINDING SITE, designated SEQ ID:8511, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48729] Another function of VGAM1389 is therefore inhibition of Phosphoinositide-3-kinase, Catalytic, Gamma Polypeptide (PIK3CG, Accession NM_002649), a gene which regulating cell growth. Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3CG. The function of PIK3CG has been established by previous studies. Phosphatidylinositol 3-kinase (PIK3) activity is implicated in diverse cellular responses triggered by mammalian cell surface receptors. Stoyanov et al. (1995) noted that receptors with tyrosine kinase activity recruit heterodimeric PIK3 kinases composed of a p110 catalytic subunit and a p85 adaptor subunit (OMIM Ref. No. 171833). Stoyanov et al. (1995) screened a human bone marrow cDNA library with primers based on the sequences of yeast and bovine PIK3 p110 subunits. They isolated a human cDNA for a novel p110 subunit, which they termed p110-gamma. The

cDNA encodes a predicted 120-kD, 1,050-amino acid polypeptide with 36% identity to human p110- α (OMIM Ref. No. 171834). The 5.3-kb p110- α transcript was detectable by Northern blot in human pancreas, skeletal muscle, liver, and heart. Stoyanov et al. (1995) found that recombinant p110- γ did not interact with the p85 subunit in vivo, in contrast to recombinant p110- α . The transducin G protein subunits G- β (t) (OMIM Ref. No. 189974)/G- γ (t) (OMIM Ref. No. 189970) did, however, activate p110- γ in vitro, and the stimulation was suppressed by G- α (t)-GDP (OMIM Ref. No. 139330); G- α (t)-GDP could stimulate p110- γ only in the presence of AlF(4-). In contrast, the p85-dependent p110- α was not similarly affected by the G protein subunits. Stoyanov et al. (1995) speculated that the p110- γ isotype may link signaling through G protein-coupled receptors and generate phosphoinositide second messengers phosphorylated in the D-3 position. Animal model experiments lend further support to the function of PI3K- γ . Hirsch et al. (2000), Sasaki et al. (2000), and Li et al. (2000) each independently developed mice deficient in PI3K- γ by targeted disruption. PI3K- γ -/- mice were viable and had fully dif-

ferentiated neutrophils and macrophages. Chemoattractant-stimulated PI3K-gamma $-/-$ neutrophils did not produce phosphatidylinositol 3,4,5-triphosphate, did not activate protein kinase B, and displayed impaired respiratory burst and motility. Peritoneal PI3K-gamma-null macrophages showed a reduced migration toward a wide range of chemotactic stimuli and a severely defective accumulation in a septic peritonitis model, as shown by Hirsch et al. (2000). These results demonstrated that PI3K-gamma is a crucial signaling molecule required for macrophage accumulation in inflammation. Sasaki et al. (2000) demonstrated that PI3K-gamma controls thymocyte survival and activation of mature T cells, but has no role in the development or function of B cells.

PI3K-gamma-deficient neutrophils exhibited severe defects in migration and respiratory burst in response to G protein-coupled receptor agonists and chemotactic agents. PI3K-gamma links G protein-coupled receptor stimulation to the formation of phosphatidylinositol 3,4,5-triphosphate and the activation of protein kinase B, ribosomal protein S6 kinase (see OMIM Ref. No. 300075), and extracellular signal-regulated kinases 1 (OMIM Ref. No. 601795) and 2. Thus, Sasaki et al. (2000) concluded

that PI3K-gamma regulates thymocyte development, T-cell activation, neutrophil migration, and the oxidative burst. Li et al. (2000) reported similar results and also found that PI3K-gamma has an important role in chemoattractant-induced superoxide production and chemotaxis and in the production of T cell-independent antigen-specific antibodies composed of the immunoglobulin-gamma light chain

[48730] It is appreciated that the abovementioned animal model for PIK3CG is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[48731] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48732] Stoyanov, B.; Volinia, S.; Hanck, T.; Rubio, I.; Loubtchenkov, M.; Malek, D.; Stoyanova, S.; Vanhaesebroeck, B.; Dhand, R.; Nurnberg, B.; Gierschik, P.; Seedorf, K.; Hsuan, J. J.; Waterfield, M. D.; Wetzker, R. : Cloning and characterization of a G protein-activated human phosphoinositide-3 kinase. Science 269: 690-693, 1995. ; and

[48733] Li, Z.; Jiang, H.; Xie, W.; Zhang, Z.; Smrcka, A. V.; Wu, D. : Roles of PLC-beta-2 and -beta-3 and PI3K-gamma in

chemoattractant-mediated signal transduction. Science 287: 1046-1049, 2000.

[48734] Further studies establishing the function and utilities of PIK3CG are found in John Hopkins OMIM database record ID 601232, and in cited publications numbered 9852-9855, 6842, 786 and 10854-2833 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ13449 (Accession NM_024546) is another VGAM1389 host target gene. FLJ13449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13449 BINDING SITE, designated SEQ ID:23759, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48735] Another function of VGAM1389 is therefore inhibition of FLJ13449 (Accession NM_024546). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13449. KIAA1025 (Accession XM_034056) is another VGAM1389 host target gene. KIAA1025 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1025 BINDING SITE, designated SEQ ID:31995, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48736] Another function of VGAM1389 is therefore inhibition of KIAA1025 (Accession XM_034056). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1025. Protocadherin 17 (PCDH17, Accession NM_014459) is another VGAM1389 host target gene. PCDH17 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH17 BINDING SITE, designated SEQ ID:15811, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48737] Another function of VGAM1389 is therefore inhibition of Protocadherin 17 (PCDH17, Accession NM_014459). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH17. Zinc Finger Protein 384 (ZNF384, Accession NM_133476) is another VGAM1389 host target gene. ZNF384 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF384, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF384 BINDING SITE, designated SEQ ID:28542, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48738] Another function of VGAM1389 is therefore inhibition of Zinc Finger Protein 384 (ZNF384, Accession NM_133476). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF384. LOC166042 (Accession XM_093623) is another VGAM1389 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40199, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48739] Another function of VGAM1389 is therefore inhibition of LOC166042 (Accession XM_093623). Accordingly, utilities of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC222662 (Accession XM_167086) is another VGAM1389 host target gene. LOC222662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222662 BINDING SITE, designated SEQ ID:44601, to the nucleotide sequence of VGAM1389 RNA, herein designated VGAM RNA, also designated SEQ ID:4100.

[48740] Another function of VGAM1389 is therefore inhibition of LOC222662 (Accession XM_167086). Accordingly, utilities

of VGAM1389 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222662. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1390 (VGAM1390) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48741] VGAM1390 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1390 was detected is described hereinabove with reference to Figs. 1-8.

[48742] VGAM1390 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cercopithecine Herpesvirus 7. VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48743] VGAM1390 gene encodes a VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1390 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1390 precursor RNA is designated SEQ ID:1376, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1376 is located at position 57196 relative to the genome of Cercopithecine Herpesvirus 7.

- [48744] VGAM1390 precursor RNA folds onto itself, forming VGAM1390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48745] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1390 folded precursor RNA into VGAM1390 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1390 RNA is designated SEQ ID:4101, and

is provided hereinbelow with reference to the sequence listing part.

[48746] VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1390 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[48747] VGAM1390 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1390 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1390 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48748] The complementary binding of VGAM1390 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1390 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1390 host target RNA into VGAM1390 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48749] It is appreciated that VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1390 host target genes. The mRNA of each one of this plurality of VGAM1390 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1390 RNA, herein designated VGAM RNA, and which when bound by VGAM1390 RNA causes inhibition of translation of respective one or more VGAM1390 host target proteins.

[48750] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1390 gene, herein designated VGAM GENE, on one or more VGAM1390 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48751] It is yet further appreciated that a function of VGAM1390 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM1390 correlate with, and may be deduced from, the identity of the host target genes which VGAM1390 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48752] Nucleotide sequences of the VGAM1390 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1390 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1390 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1390 are further described hereinbelow with reference to Table 1.

[48753] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1390 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1390 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48754] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1390 gene, herein designated VGAM is inhibition of expression of VGAM1390 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1390 correlate with, and may be deduced from, the identity of the target genes which VGAM1390 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48755] Calumenin (CALU, Accession NM_001219) is a VGAM1390 host target gene. CALU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALU BINDING SITE, designated SEQ ID:6886, to the nucleotide sequence of VGAM1390 RNA, herein designated VGAM RNA, also designated SEQ ID:4101.

[48756] A function of VGAM1390 is therefore inhibition of Calumenin (CALU, Accession NM_001219), a gene which binds 7 calcium ions with a low affinity with unidentified function. Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALU. The function of CALU and its

association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM253. Eukaryotic Translation Initiation Factor 2- α Kinase 3 (EIF2AK3, Accession NM_004836) is another VGAM1390 host target gene. EIF2AK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2AK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2AK3 BINDING SITE, designated SEQ ID:11245, to the nucleotide sequence of VGAM1390 RNA, herein designated VGAM RNA, also designated SEQ ID:4101.

[48757] Another function of VGAM1390 is therefore inhibition of Eukaryotic Translation Initiation Factor 2- α Kinase 3 (EIF2AK3, Accession NM_004836). Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2AK3. Peroxisomal Biogenesis Factor 3 (PEX3, Accession NM_003630) is another VGAM1390 host target gene. PEX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEX3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEX3 BINDING SITE, designated SEQ ID:9691, to the nucleotide sequence of VGAM1390 RNA, herein designated VGAM RNA, also designated SEQ ID:4101.

[48758] Another function of VGAM1390 is therefore inhibition of Peroxisomal Biogenesis Factor 3 (PEX3, Accession NM_003630). Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEX3. Single-minded Homolog 1 (Drosophila) (SIM1, Accession NM_005068) is another VGAM1390 host target gene. SIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIM1 BINDING SITE, designated SEQ ID:11509, to the nucleotide sequence of VGAM1390 RNA, herein designated VGAM RNA, also designated SEQ ID:4101.

[48759] Another function of VGAM1390 is therefore inhibition of Single-minded Homolog 1 (Drosophila) (SIM1, Accession

NM_005068), a gene which may have pleiotropic effects during embryogenesis and in the adult. Accordingly, utilities of VGAM1390 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIM1. The function of SIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM665. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1391 (VGAM1391) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48760] VGAM1391 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1391 was detected is described hereinabove with reference to Figs. 1–8.

[48761] VGAM1391 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Wheat Streak Mosaic Virus. VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48762] VGAM1391 gene encodes a VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1391 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1391 precursor RNA is designated SEQ ID:1377, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1377 is located at position 6460 relative to the genome of Wheat Streak Mosaic Virus.

[48763] VGAM1391 precursor RNA folds onto itself, forming VGAM1391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48764] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1391 folded precursor RNA into VGAM1391 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM1391 RNA is designated SEQ ID:4102, and is provided hereinbelow with reference to the sequence listing part.

[48765] VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1391 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48766] VGAM1391 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1391 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1391 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48767] The complementary binding of VGAM1391 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1391 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1391 host target RNA into VGAM1391 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48768] It is appreciated that VGAM1391 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1391 host target genes. The mRNA of each one of this plurality of VGAM1391 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1391 RNA, herein designated VGAM RNA, and which when bound by VGAM1391 RNA causes inhibition of translation of respective one or more VGAM1391 host target proteins.

[48769] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1391 gene, herein designated VGAM GENE, on one or more VGAM1391 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[48770] It is yet further appreciated that a function of VGAM1391 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of viral infection by Wheat Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1391 correlate with, and may be deduced from, the identity of the host target genes which VGAM1391 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48771] Nucleotide sequences of the VGAM1391 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1391 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1391 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1391 are further described hereinbelow with reference to Table 1.

[48772] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1391 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1391 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48773] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1391 gene, herein designated VGAM is inhibition of expression of VGAM1391 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1391 correlate with, and may be deduced from, the identity of the target genes which VGAM1391 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48774] ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164) is a VGAM1391 host target gene. ABCD2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD2 BINDING SITE, designated SEQ ID:11659, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48775] A function of VGAM1391 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164), a gene which probable transporter. Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD2. The function of ABCD2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229.RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession NM_133509) is another VGAM1391 host target gene. RAD51L1 BINDING SITE1 and RAD51L1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD51L1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD51L1 BINDING SITE1 and RAD51L1 BINDING SITE2, designated SEQ ID:28576 and SEQ ID:8787 respectively, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48776] Another function of VGAM1391 is therefore inhibition of RAD51-like 1 (*S. cerevisiae*) (RAD51L1, Accession

NM_133509), a gene which is a member of the RAD51 family of strand-transfer proteins. Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD51L1. The function of RAD51L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1020.DKFZP434C212 (Accession XM_044196) is another VGAM1391 host target gene. DKFZP434C212 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C212 BINDING SITE, designated SEQ ID:34170, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48777] Another function of VGAM1391 is therefore inhibition of DKFZP434C212 (Accession XM_044196). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434C212. DKFZP566J091 (Accession

NM_030915) is another VGAM1391 host target gene. DKFZP566J091 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566J091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566J091 BINDING SITE, designated SEQ ID:25184, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48778] Another function of VGAM1391 is therefore inhibition of DKFZP566J091 (Accession NM_030915). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566J091. FLJ22419 (Accession NM_024697) is another VGAM1391 host target gene. FLJ22419 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22419, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22419 BINDING SITE, designated SEQ ID:24006, to the nucleotide sequence of VGAM1391 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4102.

[48779] Another function of VGAM1391 is therefore inhibition of FLJ22419 (Accession NM_024697). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22419. HSPC055 (Accession NM_014153) is another VGAM1391 host target gene. HSPC055 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPC055, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC055 BINDING SITE, designated SEQ ID:15436, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48780] Another function of VGAM1391 is therefore inhibition of HSPC055 (Accession NM_014153). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC055. IL-17RE (Accession NM_144640) is another VGAM1391 host target gene. IL-17RE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL-17RE, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL-17RE BINDING SITE, designated SEQ ID:29464, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48781] Another function of VGAM1391 is therefore inhibition of IL-17RE (Accession NM_144640). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL-17RE. KIAA0057 (Accession NM_012288) is another VGAM1391 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14619, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48782] Another function of VGAM1391 is therefore inhibition of KIAA0057 (Accession NM_012288). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA0057. KIAA0447 (Accession XM_049733) is another VGAM1391 host target gene. KIAA0447 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35493, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48783] Another function of VGAM1391 is therefore inhibition of KIAA0447 (Accession XM_049733). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. KIAA1855 (Accession XM_166453) is another VGAM1391 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44350, to the

nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48784] Another function of VGAM1391 is therefore inhibition of KIAA1855 (Accession XM_166453). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. KIAA1871 (Accession XM_028409) is another VGAM1391 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30703, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48785] Another function of VGAM1391 is therefore inhibition of KIAA1871 (Accession XM_028409). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. MGC32104 (Accession NM_144684) is another VGAM1391 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29503, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48786] Another function of VGAM1391 is therefore inhibition of MGC32104 (Accession NM_144684). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. RPH3A (Accession NM_014954) is another VGAM1391 host target gene. RPH3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPH3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPH3A BINDING SITE, designated SEQ ID:17308, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48787] Another function of VGAM1391 is therefore inhibition of RPH3A (Accession NM_014954). Accordingly, utilities of

VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPH3A. LOC121838 (Accession XM_071772) is another VGAM1391 host target gene. LOC121838 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC121838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121838 BINDING SITE, designated SEQ ID:37416, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48788] Another function of VGAM1391 is therefore inhibition of LOC121838 (Accession XM_071772). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121838. LOC145980 (Accession XM_096914) is another VGAM1391 host target gene. LOC145980 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145980 BINDING SITE, designated SEQ ID:40648, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48789] Another function of VGAM1391 is therefore inhibition of LOC145980 (Accession XM_096914). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145980. LOC149703 (Accession XM_097719) is another VGAM1391 host target gene. LOC149703 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149703, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149703 BINDING SITE, designated SEQ ID:41062, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48790] Another function of VGAM1391 is therefore inhibition of LOC149703 (Accession XM_097719). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149703. LOC170395 (Accession XM_084325) is another VGAM1391 host target gene. LOC170395 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170395 BINDING SITE, designated SEQ ID:37545, to the nucleotide sequence of VGAM1391 RNA, herein designated VGAM RNA, also designated SEQ ID:4102.

[48791] Another function of VGAM1391 is therefore inhibition of LOC170395 (Accession XM_084325). Accordingly, utilities of VGAM1391 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170395. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1392 (VGAM1392) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48792] VGAM1392 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1392 was detected is described hereinabove with reference to Figs. 1-8.

[48793] VGAM1392 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Wheat Streak Mosaic Virus. VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48794] VGAM1392 gene encodes a VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1392 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1392 precursor RNA is designated SEQ ID:1378, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1378 is located at position 9058 relative to the genome of Wheat Streak Mosaic Virus.

[48795] VGAM1392 precursor RNA folds onto itself, forming VGAM1392 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[48796] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1392 folded precursor RNA into VGAM1392 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1392 RNA is designated SEQ ID:4103, and is provided hereinbelow with reference to the sequence listing part.

[48797] VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1392 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48798] VGAM1392 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1392 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1392 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1392 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[48799] The complementary binding of VGAM1392 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1392 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1392 host target RNA into VGAM1392 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48800] It is appreciated that VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1392 host target genes. The mRNA of each one of this plurality of VGAM1392 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1392 RNA, herein designated VGAM RNA, and which when bound by VGAM1392 RNA causes inhibition of translation of respective one or more VGAM1392 host target proteins.

[48801] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1392 gene, herein designated VGAM GENE, on one or more VGAM1392 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48802] It is yet further appreciated that a function of VGAM1392 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of viral infection by Wheat Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1392 correlate with, and may be deduced from, the identity of the host target genes which VGAM1392 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48803] Nucleotide sequences of the VGAM1392 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1392 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1392 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1392 are further described hereinbelow with reference to Table 1.

[48804] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1392 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1392 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48805] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1392 gene, herein designated VGAM is inhibition of expression of VGAM1392 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1392 correlate with, and may be deduced from, the identity of the target genes which VGAM1392 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48806] A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM_139275) is a VGAM1392 host target gene. AKAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of AKAP1 BINDING SITE, designated SEQ ID:29266, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48807] A function of VGAM1392 is therefore inhibition of A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM_139275), a gene which binds to type i and ii regulatory subunits of protein kinase a . Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP1. The function of AKAP1 has been established by previous studies. In eukaryotic cells, cytosolic cAMP activates several isoforms of cAMP-dependent protein kinases (PKAs) involved in signal transduction. PKAs are composed of 2 regulatory and 2 catalytic subunits (see OMIM Ref. No. 176911). There are 2 classes of regulatory subunits: type I, which is found primarily in cytoplasmic PKAs, and type II, a significant proportion of which is found in PKAs associated with the particulate fraction of cell homogenates. The effects of individual PKA isoforms are determined by their cellular localization, specified through binding to distinct AKAPs, named for 'A-kinase anchor protein.' Anchoring proteins target the kinase by tethering a regula-

tory subunit. Trendelenburg et al. (1996) cloned AKAP149 using an antiserum to screen a human colon cDNA expression library. The cDNA sequence of AKAP149 predicted a polypeptide of 903 amino acids with a predicted mass of 97 kD. The authors noted that a portion of the cDNA sequence of AKAP149 is identical to S-AKAP84, previously described by Lin et al. (1995). The first 517 amino acids of the sequence of AKAP149 is identical to those of the S-AKAP84 sequence (except at amino acid positions 97 and 98), including a signal sequence.

AKAP149 also has a protein/serine/threonine-rich region at amino acids 489–540, and a K-homologous (KH) motif at amino acids 612–659. Trendelenburg et al. (1996) suggested that AKAP149 and S-AKAP84 are splice variants of the same gene. The KH motif is an RNA-binding domain typically associated with proteins involved in RNA catalysis, mRNA processing, or translation. By Southern blotting, Trendelenburg et al. (1996) showed that AKAP149 is a single-copy gene in the human genome. By Northern blot analysis, they showed that AKAP149 was expressed as a 4.2-kb transcript in all epithelial tissues examined, with the strongest signal being detected in prostate and small intestine RNAs. In addition, a 3.2-kb transcript was

expressed exclusively in testis. Lin et al. (1995) found a similar pattern of expression for S-AKAP84, but also detected a minor 7.5-kb transcript in kidney, pancreas, liver, lung, and brain. By Western blotting, Trendelenburg et al. (1996) detected expression of the AKAP149 protein in colon carcinoma LS174T cells. Trendelenburg et al. (1996) speculated that AKAP149 is involved in the cAMP-dependent signal transduction pathway and in directing RNA to a specific cellular compartment. Huang et al. (1997) cloned cDNAs encoding a possible mouse homolog of S-AKAP84. Since the protein bound both PKA type I and type II regulatory subunits, they designated the gene D-Akap1 for 'dual specificity Akap1.' Previously identified AKAPs had interacted specifically with type II subunits. Northern blot analysis detected D-Akap1 expression in all tissues examined except the spleen. Huang et al. (1997) isolated cDNAs representing at least 4 splice variants. By Western blot analysis, they showed that the different protein isoforms may be expressed in a tissue-specific manner. The mitochondria target/signal region found in both S-Akap84 and D-Akap1 suggested to Huang et al. (1997) that some of the protein isoforms may be targeted to the mitochondria.

[48808] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48809] Trendelenburg, G.; Hummel, M.; Riecken, E.-O.; Hanski, C. : Molecular characterization of AKAP149, a novel A kinase anchor protein with a KH domain. *Biochem. Biophys. Res. Commun.* 225: 313–319, 1996. ; and

[48810] Huang, L. J.; Durick, K.; Weiner, J. A.; Chun, J.; Taylor, S. S. : Identification of a novel protein kinase A anchoring protein that binds both type I and type II regulatory subunits. *J.*

[48811] Further studies establishing the function and utilities of AKAP1 are found in John Hopkins OMIM database record ID 602449, and in cited publications numbered 6316–6318 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hepatic Leukemia Factor (HLF, Accession NM_002126) is another VGAM1392 host target gene. HLF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLF BINDING SITE, design-

nated SEQ ID:7904, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48812] Another function of VGAM1392 is therefore inhibition of Hepatic Leukemia Factor (HLF, Accession NM_002126). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLF. Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499) is another VGAM1392 host target gene. NEO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEO1 BINDING SITE, designated SEQ ID:8317, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48813] Another function of VGAM1392 is therefore inhibition of Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499), a gene which regulates the transition of undifferentiated proliferating cells to their differentiated state. Accordingly, utilities of VGAM1392 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with NEO1. The function of NEO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM329. Phosphomannomutase 2 (PMM2, Accession XM_050755) is another VGAM1392 host target gene.

PMM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMM2 BINDING SITE, designated SEQ ID:35680, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48814] Another function of VGAM1392 is therefore inhibition of Phosphomannomutase 2 (PMM2, Accession XM_050755). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMM2. Titin (TTN, Accession NM_133378) is another VGAM1392 host target gene. TTN BINDING SITE1 through TTN BINDING SITE3 are HOST

TARGET binding sites found in untranslated regions of mRNA encoded by TTN, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTN BINDING SITE1 through TTN BINDING SITE3, designated SEQ ID:28502, SEQ ID:28507 and SEQ ID:28517 respectively, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48815] Another function of VGAM1392 is therefore inhibition of Titin (TTN, Accession NM_133378). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTN. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_003671) is another VGAM1392 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ ID:9761, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM

RNA, also designated SEQ ID:4103.

[48816] Another function of VGAM1392 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_003671). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. FLJ13441 (Accession NM_023924) is another VGAM1392 host target gene. FLJ13441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13441 BINDING SITE, designated SEQ ID:23392, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48817] Another function of VGAM1392 is therefore inhibition of FLJ13441 (Accession NM_023924). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13441. FLJ22529 (Accession NM_024789) is another VGAM1392 host target gene. FLJ22529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22529 BINDING SITE, designated SEQ ID:24171, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48818] Another function of VGAM1392 is therefore inhibition of FLJ22529 (Accession NM_024789). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22529. KIAA0738 (Accession NM_014719) is another VGAM1392 host target gene. KIAA0738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0738 BINDING SITE, designated SEQ ID:16279, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48819] Another function of VGAM1392 is therefore inhibition of KIAA0738 (Accession NM_014719). Accordingly, utilities

of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0738. KIAA1764 (Accession XM_045086) is another VGAM1392 host target gene. KIAA1764 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1764 BINDING SITE, designated SEQ ID:34354, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48820] Another function of VGAM1392 is therefore inhibition of KIAA1764 (Accession XM_045086). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1764. LAGY (Accession NM_139211) is another VGAM1392 host target gene. LAGY BINDING SITE1 through LAGY BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LAGY, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of LAGY BINDING SITE1 through LAGY BINDING SITE3, designated SEQ ID:29231, SEQ ID:29233 and SEQ ID:26245 respectively, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48821] Another function of VGAM1392 is therefore inhibition of LAGY (Accession NM_139211). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAGY. Mitochondrial Ribosomal Protein S11 (MRPS11, Accession XM_170552) is another VGAM1392 host target gene. MRPS11 BINDING SITE1 and MRPS11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MRPS11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS11 BINDING SITE1 and MRPS11 BINDING SITE2, designated SEQ ID:45377 and SEQ ID:12493 respectively, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48822] Another function of VGAM1392 is therefore inhibition of Mitochondrial Ribosomal Protein S11 (MRPS11, Accession

XM_170552). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS11. LOC150622 (Accession XM_086960) is another VGAM1392 host target gene. LOC150622 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150622 BINDING SITE, designated SEQ ID:38996, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48823] Another function of VGAM1392 is therefore inhibition of LOC150622 (Accession XM_086960). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150622. LOC196540 (Accession XM_116933) is another VGAM1392 host target gene. LOC196540 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC196540 BINDING SITE, designated SEQ ID:43150, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48824] Another function of VGAM1392 is therefore inhibition of LOC196540 (Accession XM_116933). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196540. LOC200047 (Accession XM_114099) is another VGAM1392 host target gene. LOC200047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200047 BINDING SITE, designated SEQ ID:42698, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48825] Another function of VGAM1392 is therefore inhibition of LOC200047 (Accession XM_114099). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200047. LOC92597 (Accession XM_046066) is an-

other VGAM1392 host target gene. LOC92597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92597 BINDING SITE, designated SEQ ID:34671, to the nucleotide sequence of VGAM1392 RNA, herein designated VGAM RNA, also designated SEQ ID:4103.

[48826] Another function of VGAM1392 is therefore inhibition of LOC92597 (Accession XM_046066). Accordingly, utilities of VGAM1392 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1393 (VGAM1393) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48827] VGAM1393 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1393 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[48828] VGAM1393 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Wheat Streak Mosaic Virus. VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48829] VGAM1393 gene encodes a VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1393 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1393 precursor RNA is designated SEQ ID:1379, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1379 is located at position 3923 relative to the genome of Wheat Streak Mosaic Virus.

[48830] VGAM1393 precursor RNA folds onto itself, forming VGAM1393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48831] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1393 folded precursor RNA into VGAM1393 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1393 RNA is designated SEQ ID:4104, and is provided hereinbelow with reference to the sequence listing part.

[48832] VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1393 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48833] VGAM1393 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1393 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1393 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1393 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48834] The complementary binding of VGAM1393 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1393 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1393 host target RNA into VGAM1393 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48835] It is appreciated that VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1393 host target genes. The mRNA of each one of this plurality of VGAM1393 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1393 RNA, herein designated VGAM RNA, and which when bound by VGAM1393 RNA causes inhibition of translation of respective one or more VGAM1393 host target proteins.

[48836] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1393 gene, herein designated VGAM GENE, on one or more VGAM1393 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48837] It is yet further appreciated that a function of VGAM1393 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of viral infection by Wheat Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1393 correlate with, and may be deduced from, the identity of the host target genes which VGAM1393 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48838] Nucleotide sequences of the VGAM1393 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1393 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1393 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1393 are further described hereinbelow with reference to Table 1.

[48839] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1393 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1393 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48840] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1393 gene, herein designated VGAM is inhibition of expression of VGAM1393 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1393 correlate with, and may be deduced from, the identity of the target genes which VGAM1393 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48841] Chloride Channel, Calcium Activated, Family Member 3 (CLCA3, Accession NM_004921) is a VGAM1393 host target gene. CLCA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLCA3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCA3 BINDING SITE, designated SEQ ID:11354, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48842] A function of VGAM1393 is therefore inhibition of Chloride Channel, Calcium Activated, Family Member 3 (CLCA3, Accession NM_004921), a gene which is similar to calcium-activated chloride channel family. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLCA3. The function of CLCA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM595. Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM_005670) is another VGAM1393 host target gene. EPM2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPM2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of EPM2A BINDING SITE, designated SEQ ID:12224, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48843] Another function of VGAM1393 is therefore inhibition of Epilepsy, Progressive Myoclonus Type 2, Lafora Disease (laforin) (EPM2A, Accession NM_005670), a gene which Laforin; protein tyrosine phosphatase that may have role in glycogen metabolism. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPM2A. The function of EPM2A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM470. Melanoma Antigen, Family A, 10 (MAGEA10, Accession NM_021048) is another VGAM1393 host target gene. MAGEA10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAGEA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGEA10 BINDING SITE, designated SEQ ID:22034, to the nucleotide sequence of VGAM1393

RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48844] Another function of VGAM1393 is therefore inhibition of Melanoma Antigen, Family A, 10 (MAGEA10, Accession NM_021048), a gene which may play a role in embryonal development and tumor transformation or aspects of tumor progression. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGEA10. The function of MAGEA10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926) is another VGAM1393 host target gene. MBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD3 BINDING SITE, designated SEQ ID:10020, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48845] Another function of VGAM1393 is therefore inhibition of

Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926), a gene which are subunits of the NURD (nucleosome remodeling and histone deacetylase) complex . Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD3. The function of MBD3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM247. Protocadherin 11 X-linked (PCDH11X, Accession NM_032969) is another VGAM1393 host target gene. PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH11X, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH11X BINDING SITE1 and PCDH11X BINDING SITE2, designated SEQ ID:26799 and SEQ ID:26784 respectively, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48846] Another function of VGAM1393 is therefore inhibition of Protocadherin 11 X-linked (PCDH11X, Accession

NM_032969), a gene which is thought to play a fundamental role in cell-cell recognition essential for the segmental development and function of the central nervous system. Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH11X. The function of PCDH11X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.SMG1 (Accession NM_015092) is another VGAM1393 host target gene. SMG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMG1 BINDING SITE, designated SEQ ID:17477, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48847] Another function of VGAM1393 is therefore inhibition of SMG1 (Accession NM_015092), a gene which acts as the target for the cell-cycle arrest and immunosuppressive effects. Accordingly, utilities of VGAM1393 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with SMG1. The function of SMG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419.AD-020 (Accession NM_020141) is another VGAM1393 host target gene. AD-020 BINDING SITE1 and AD-020 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AD-020, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AD-020 BINDING SITE1 and AD-020 BINDING SITE2, designated SEQ ID:21337 and SEQ ID:29867 respectively, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48848] Another function of VGAM1393 is therefore inhibition of AD-020 (Accession NM_020141). Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AD-020. FLJ00024 (Accession XM_033361) is another VGAM1393 host target gene. FLJ00024 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by FLJ00024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00024 BINDING SITE, designated SEQ ID:31893, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48849] Another function of VGAM1393 is therefore inhibition of FLJ00024 (Accession XM_033361). Accordingly, utilities of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00024. LOC203297 (Accession XM_059986) is another VGAM1393 host target gene. LOC203297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203297 BINDING SITE, designated SEQ ID:37137, to the nucleotide sequence of VGAM1393 RNA, herein designated VGAM RNA, also designated SEQ ID:4104.

[48850] Another function of VGAM1393 is therefore inhibition of LOC203297 (Accession XM_059986). Accordingly, utilities

of VGAM1393 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203297. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1394 (VGAM1394) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48851] VGAM1394 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1394 was detected is described hereinabove with reference to Figs. 1–8.

[48852] VGAM1394 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Wheat Streak Mosaic Virus. VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48853] VGAM1394 gene encodes a VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1394 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1394 precursor RNA is designated SEQ ID:1380, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1380 is located at position 2215 relative to the genome of Wheat Streak Mosaic Virus.

- [48854] VGAM1394 precursor RNA folds onto itself, forming VGAM1394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48855] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1394 folded precursor RNA into VGAM1394 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1394 RNA is designated SEQ ID:4105, and

is provided hereinbelow with reference to the sequence listing part.

[48856] VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1394 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[48857] VGAM1394 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1394 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1394 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48858] The complementary binding of VGAM1394 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1394 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1394 host target RNA into VGAM1394 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48859] It is appreciated that VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1394 host target genes. The mRNA of each one of this plurality of VGAM1394 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1394 RNA, herein designated VGAM RNA, and which when bound by VGAM1394 RNA causes inhibition of translation of respective one or more VGAM1394 host target proteins.

[48860] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1394 gene, herein designated VGAM GENE, on one or more VGAM1394 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48861] It is yet further appreciated that a function of VGAM1394 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of viral infection by Wheat Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1394 correlate with, and may be deduced from, the identity of the host target genes which VGAM1394 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48862] Nucleotide sequences of the VGAM1394 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1394 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1394 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1394 are further described hereinbelow with reference to Table 1.

[48863] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1394 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1394 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48864] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1394 gene, herein designated VGAM is inhibition of expression of VGAM1394 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1394 correlate with, and may be deduced from, the identity of the target genes which VGAM1394 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48865] Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982) is a VGAM1394 host target gene. PIK3R3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R3 BINDING SITE, designated SEQ ID:30602, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48866] A function of VGAM1394 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with PIK3R3. Sarcoglycan, Beta (43kDa dystrophin-associated glycoprotein) (SGCB, Accession NM_000232) is another VGAM1394 host target gene. SGCB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGCB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGCB BINDING SITE, designated SEQ ID:5743, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48867] Another function of VGAM1394 is therefore inhibition of Sarcoglycan, Beta (43kDa dystrophin-associated glycoprotein) (SGCB, Accession NM_000232). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGCB. Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734) is another VGAM1394 host target gene. DCAMKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCAMKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of DCAMKL1 BINDING SITE, designated SEQ ID:11112, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48868] Another function of VGAM1394 is therefore inhibition of Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCAMKL1. FLJ12517 (Accession NM_023007) is another VGAM1394 host target gene. FLJ12517 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12517, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12517 BINDING SITE, designated SEQ ID:23269, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48869] Another function of VGAM1394 is therefore inhibition of FLJ12517 (Accession NM_023007). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ12517. FLJ14936 (Accession NM_032864) is another VGAM1394 host target gene. FLJ14936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14936 BINDING SITE, designated SEQ ID:26669, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48870] Another function of VGAM1394 is therefore inhibition of FLJ14936 (Accession NM_032864). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14936. HH114 (Accession NM_032499) is another VGAM1394 host target gene. HH114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HH114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HH114 BINDING SITE, designated SEQ ID:26249, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA,

also designated SEQ ID:4105.

[48871] Another function of VGAM1394 is therefore inhibition of HH114 (Accession NM_032499). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HH114. TTY7 (Accession NM_031926) is another VGAM1394 host target gene. TTY7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTY7 BINDING SITE, designated SEQ ID:25672, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48872] Another function of VGAM1394 is therefore inhibition of TTY7 (Accession NM_031926). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTY7. LOC147054 (Accession XM_097172) is another VGAM1394 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40793, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48873] Another function of VGAM1394 is therefore inhibition of LOC147054 (Accession XM_097172). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC147929 (Accession XM_085961) is another VGAM1394 host target gene. LOC147929 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147929, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147929 BINDING SITE, designated SEQ ID:38420, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48874] Another function of VGAM1394 is therefore inhibition of LOC147929 (Accession XM_085961). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC147929. LOC90591 (Accession XM_032811) is another VGAM1394 host target gene. LOC90591 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90591, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90591 BINDING SITE, designated SEQ ID:31759, to the nucleotide sequence of VGAM1394 RNA, herein designated VGAM RNA, also designated SEQ ID:4105.

[48875] Another function of VGAM1394 is therefore inhibition of LOC90591 (Accession XM_032811). Accordingly, utilities of VGAM1394 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90591. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1395 (VGAM1395) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48876] VGAM1395 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1395 was detected is described hereinabove with reference to Figs. 1–8.

[48877] VGAM1395 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Aphid-borne Mosaic Virus. VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48878] VGAM1395 gene encodes a VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1395 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1395 precursor RNA is designated SEQ ID:1381, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1381 is located at position 3170 relative to the genome of Cowpea Aphid-borne Mosaic Virus.

[48879] VGAM1395 precursor RNA folds onto itself, forming VGAM1395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48880] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1395 folded precursor RNA into VGAM1395 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1395 RNA is designated SEQ ID:4106, and is provided hereinbelow with reference to the sequence listing part.

[48881] VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1395 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48882] VGAM1395 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1395 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1395 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48883] The complementary binding of VGAM1395 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1395 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1395 host target RNA into VGAM1395 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48884] It is appreciated that VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1395 host target genes. The mRNA of each one of this plurality of VGAM1395 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1395 RNA, herein designated VGAM RNA, and which when bound by VGAM1395 RNA causes inhibition of translation of respective one or more VGAM1395 host target proteins.

[48885] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1395 gene, herein designated VGAM GENE, on one or more VGAM1395 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48886] It is yet further appreciated that a function of VGAM1395 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of viral infection by Cowpea Aphid-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1395 correlate with, and may be deduced from, the identity of the host target genes which VGAM1395 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48887] Nucleotide sequences of the VGAM1395 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1395 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1395 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1395 are further described hereinbelow with reference to Table 1.

[48888] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1395 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1395 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48889] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1395 gene, herein designated VGAM is inhibition of expression of VGAM1395 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1395 correlate with, and may be deduced from, the identity of the target genes which VGAM1395 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48890] Chorea Acanthocytosis (CHAC, Accession NM_033305) is a VGAM1395 host target gene. CHAC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by CHAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHAC BINDING SITE, designated SEQ ID:27141, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48891] A function of VGAM1395 is therefore inhibition of Chorea Acanthocytosis (CHAC, Accession NM_033305), a gene which may regulate the cycling of proteins. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHAC. The function of CHAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM650.Epha3 (EPHA3, Accession NM_005233) is another VGAM1395 host target gene. EPHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA3 BINDING SITE, designated SEQ

ID:11739, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48892] Another function of VGAM1395 is therefore inhibition of EphA3 (EPHA3, Accession NM_005233), a gene which binds to ephrin-a2, -a3, -a4 and -a5. could play a role in lymphoid function. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA3. The function of EPHA3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164. EphB2 (EPHB2, Accession NM_004442) is another VGAM1395 host target gene. EPHB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHB2 BINDING SITE, designated SEQ ID:10729, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48893] Another function of VGAM1395 is therefore inhibition of

EphB2 (EPHB2, Accession NM_004442), a gene which Eph-related receptor tyrosine kinase B2; may have a role in neurogenesis. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHB2. The function of EPHB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM533. RAR-related Orphan Receptor B (RORB, Accession NM_006914) is another VGAM1395 host target gene. RORB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RORB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RORB BINDING SITE, designated SEQ ID:13788, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48894] Another function of VGAM1395 is therefore inhibition of RAR-related Orphan Receptor B (RORB, Accession NM_006914), a gene which is an orphan nuclear receptor. Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with RORB. The function of RORB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273) is another VGAM1395 host target gene. CHST3 BINDING SITE1 and CHST3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CHST3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST3 BINDING SITE1 and CHST3 BINDING SITE2, designated SEQ ID:10473 and SEQ ID:10481 respectively, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48895] Another function of VGAM1395 is therefore inhibition of Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST3. FLJ23042 (Accession NM_025157) is another VGAM1395 host target gene. FLJ23042 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by FLJ23042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23042 BINDING SITE, designated SEQ ID:24798, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48896] Another function of VGAM1395 is therefore inhibition of FLJ23042 (Accession NM_025157). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23042. KIAA0232 (Accession XM_052627) is another VGAM1395 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36036, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48897] Another function of VGAM1395 is therefore inhibition of

KIAA0232 (Accession XM_052627). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. KIAA0478 (Accession NM_014870) is another VGAM1395 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16973, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48898] Another function of VGAM1395 is therefore inhibition of KIAA0478 (Accession NM_014870). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA1319 (Accession NM_020770) is another VGAM1395 host target gene. KIAA1319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1319 BINDING SITE, designated SEQ ID:21865, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48899] Another function of VGAM1395 is therefore inhibition of KIAA1319 (Accession NM_020770). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1319. LOC139673 (Accession XM_071645) is another VGAM1395 host target gene. LOC139673 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139673 BINDING SITE, designated SEQ ID:37406, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48900] Another function of VGAM1395 is therefore inhibition of LOC139673 (Accession XM_071645). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139673. LOC145317 (Accession XM_096760) is an-

other VGAM1395 host target gene. LOC145317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145317 BINDING SITE, designated SEQ ID:40529, to the nucleotide sequence of VGAM1395 RNA, herein designated VGAM RNA, also designated SEQ ID:4106.

[48901] Another function of VGAM1395 is therefore inhibition of LOC145317 (Accession XM_096760). Accordingly, utilities of VGAM1395 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145317. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1396 (VGAM1396) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48902] VGAM1396 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1396 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[48903] VGAM1396 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Aphid–borne Mosaic Virus. VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48904] VGAM1396 gene encodes a VGAM1396 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1396 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1396 precursor RNA is designated SEQ ID:1382, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1382 is located at position 3478 relative to the genome of Cowpea Aphid–borne Mosaic Virus.

[48905] VGAM1396 precursor RNA folds onto itself, forming VGAM1396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48906] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1396 folded precursor RNA into VGAM1396 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1396 RNA is designated SEQ ID:4107, and is provided hereinbelow with reference to the sequence listing part.

[48907] VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1396 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48908] VGAM1396 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1396 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1396 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1396 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48909] The complementary binding of VGAM1396 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1396 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1396 host target RNA into VGAM1396 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48910] It is appreciated that VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1396 host target genes. The mRNA of each one of this plurality of VGAM1396 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1396 RNA, herein designated VGAM RNA, and which when bound by VGAM1396 RNA causes inhibition of translation of respective one or more VGAM1396 host target proteins.

[48911] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1396 gene, herein designated VGAM GENE, on one or more VGAM1396 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48912] It is yet further appreciated that a function of VGAM1396 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of viral infection by Cowpea Aphid-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1396 correlate with, and may be deduced from, the identity of the host target genes which VGAM1396 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48913] Nucleotide sequences of the VGAM1396 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1396 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1396 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1396 are further described hereinbelow with reference to Table 1.

[48914] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1396 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1396 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48915] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1396 gene, herein designated VGAM is inhibition of expression of VGAM1396 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1396 correlate with, and may be deduced from, the identity of the target genes which VGAM1396 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48916] FKRP (Accession NM_024301) is a VGAM1396 host target gene. FKRP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FKRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of FKRP BINDING SITE, designated SEQ ID:23592, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48917] A function of VGAM1396 is therefore inhibition of FKRP (Accession NM_024301). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKRP. Phosphatidylcholine Transfer Protein (PCTP, Accession NM_021213) is another VGAM1396 host target gene. PCTP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTP BINDING SITE, designated SEQ ID:22193, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48918] Another function of VGAM1396 is therefore inhibition of Phosphatidylcholine Transfer Protein (PCTP, Accession NM_021213), a gene which catalyzes the transfer of phosphatidylcholine between membranes (by similarity). Accordingly, utilities of VGAM1396 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with PCTP. The function of PCTP has been established by previous studies. Phosphatidylcholine (PC) transfer protein (PCTP) is a cytosolic protein first purified from bovine and rat liver that catalyzes intermembrane transfer of PC. By searching an EST database for homologs of bovine Pctp, followed by 5-prime RACE and PCR of a kidney cDNA library, Cohen et al. (1999) obtained a cDNA encoding human PCTP. The deduced 214-amino acid human protein is 76% and 80% identical to bovine and rat Pctp, respectively. Northern blot analysis revealed wide expression of an approximately 2.3-kb PCTP transcript in all tissues tested except thymus. Highest expression was detected in liver, placenta, testis, kidney, and heart, and lowest levels were found in brain and lung. Animal model experiments lend further support to the function of PCTP. Van Helvoort et al. (1999) disrupted the Pctp gene in mice. Pctp knockout mice showed no defects in the secretion of PC into bile or lung surfactant, and the lipid content and composition of bile and surfactant was normal. The authors concluded that PCTP does not play a major role in transporting PC from the endoplasmic reticulum, where it is synthesized, to the hepatocyte canalicular membrane.

[48919] It is appreciated that the abovementioned animal model for PCTP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[48920] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48921] Cohen, D. E.; Green, R. M.; Wu, M. K.; Beier, D. R. : Cloning, tissue-specific expression, gene structure and chromosomal localization of human phosphatidylcholine transfer protein. *Biochim. Biophys. Acta* 1447: 265–270, 1999. ; and

[48922] van Helvoort, A.; de Brouwer, A.; Ottenhoff, R.; Brouwers, J. F. H. M.; Wijnholds, J.; Beijnen, J. H.; Rijneveld, A.; van der Valk, M. A.; Majoor, D.; Voorhout, W.; Wirtz, K. W. A.; El.

[48923] Further studies establishing the function and utilities of PCTP are found in John Hopkins OMIM database record ID 606055, and in cited publications numbered 6826–6827 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Renal Tumor Antigen (RAGE, Accession NM_014226) is another VGAM1396 host target gene. RAGE BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by RAGE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAGE BINDING SITE, designated SEQ ID:15495, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48924] Another function of VGAM1396 is therefore inhibition of Renal Tumor Antigen (RAGE, Accession NM_014226), a gene which is essential for the completion of the start, the controlling event, in the cell cycle. Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAGE. The function of RAGE has been established by previous studies. Sugaya et al. (1994) identified 3 genes located 90 to 140 kb centromeric to the tenascin-like gene (OMIM Ref. No. 600261) in the MHC class III region near the junction with class II. One of these was the gene for receptor of advanced glycosylation end products of proteins, a member of the immunoglobulin superfamily. A second was the PBX2 homeo box gene (OMIM Ref. No. 176311), and a third was the human counterpart of the

mouse mammary tumor gene int-3 (OMIM Ref. No. 164951). The PBX2 and AGER genes are immediately contiguous and are transcribed in the same direction. In addition to mapping by contiguous cosmids and YAC clones, Sugaya et al. (1994) determined the location of the AGER sequence on 6p21.3 by fluorescence in situ hybridization. Yan et al. (1996) reported that the AGER protein, called RAGE (receptor for advanced glycation end products) by them, is an important receptor for the amyloid beta peptide (OMIM Ref. No. 104760) and that expression of this receptor increases in Alzheimer disease (OMIM Ref. No. 104300). They noted that expression of RAGE is particularly increased in neurons close to deposits of amyloid beta peptide and to neurofibrillary tangles.

[48925] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48926] Sugaya, K.; Fukagawa, T.; Matsumoto, K.; Mita, K.; Takahashi, E.; Ando, A.; Inoko, H.; Ikemura, T. : Three genes in the human MHC class III region near the junction with the class II: gene for receptor of advanced glycosylation end products, PBX2 homeobox gene and a Notch homolog, human counterpart of mouse mammary tumor gene int-3.

Genomics 23: 408–419, 1994. ; and

[48927] Yan, S. D.; Chen, X.; Fu, J.; Chen, M.; Zhu, H.; Roher, A.;
Slattery, T.; Zhao, L.; Nagashima, M.; Morser, J.; Migheli,
A.; Nawroth, P.; Stern, D.; Schmidt, A. M. : RAGE and amy-
loid-beta.

[48928] Further studies establishing the function and utilities of RAGE are found in John Hopkins OMIM database record ID 600214, and in cited publications numbered 10683, 1080 and 10684 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine/threonine Kinase 31 (STK31, Accession NM_032944) is another VGAM1396 host target gene. STK31 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STK31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK31 BINDING SITE, designated SEQ ID:26761, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48929] Another function of VGAM1396 is therefore inhibition of Serine/threonine Kinase 31 (STK31, Accession NM_032944). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK31. KIAA0293 (Accession XM_027045) is another VGAM1396 host target gene. KIAA0293 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by KIAA0293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0293 BINDING SITE, designated SEQ ID:30396, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48930] Another function of VGAM1396 is therefore inhibition of KIAA0293 (Accession XM_027045). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0293. KIAA1023 (Accession NM_017604) is another VGAM1396 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19088, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48931] Another function of VGAM1396 is therefore inhibition of

KIAA1023 (Accession NM_017604). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. MGC16384 (Accession NM_053048) is another VGAM1396 host target gene. MGC16384 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16384, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16384 BINDING SITE, designated SEQ ID:27593, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48932] Another function of VGAM1396 is therefore inhibition of MGC16384 (Accession NM_053048). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16384. MGC16386 (Accession NM_080668) is another VGAM1396 host target gene. MGC16386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of MGC16386 BINDING SITE, designated SEQ ID:27958, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48933] Another function of VGAM1396 is therefore inhibition of MGC16386 (Accession NM_080668). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16386. MGC4549 (Accession NM_032377) is another VGAM1396 host target gene. MGC4549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4549 BINDING SITE, designated SEQ ID:26171, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48934] Another function of VGAM1396 is therefore inhibition of MGC4549 (Accession NM_032377). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4549. Synaptopodin 2 (SYNPO2, Accession

XM_050219) is another VGAM1396 host target gene.

SYNPO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNPO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNPO2 BINDING SITE, designated SEQ ID:35593, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48935] Another function of VGAM1396 is therefore inhibition of Synaptopodin 2 (SYNPO2, Accession XM_050219). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNPO2. LOC146229 (Accession XM_085387) is another VGAM1396 host target gene. LOC146229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146229 BINDING SITE, designated SEQ ID:38108, to the nucleotide sequence of VGAM1396 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4107.

[48936] Another function of VGAM1396 is therefore inhibition of LOC146229 (Accession XM_085387). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146229. LOC151816 (Accession XM_098122) is another VGAM1396 host target gene. LOC151816 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151816 BINDING SITE, designated SEQ ID:41390, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48937] Another function of VGAM1396 is therefore inhibition of LOC151816 (Accession XM_098122). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151816. LOC154449 (Accession XM_087928) is another VGAM1396 host target gene. LOC154449 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154449, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154449 BINDING SITE, designated SEQ ID:39476, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48938] Another function of VGAM1396 is therefore inhibition of LOC154449 (Accession XM_087928). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154449. LOC155179 (Accession XM_088169) is another VGAM1396 host target gene. LOC155179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155179 BINDING SITE, designated SEQ ID:39555, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48939] Another function of VGAM1396 is therefore inhibition of LOC155179 (Accession XM_088169). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC155179. LOC158056 (Accession XM_088463) is another VGAM1396 host target gene. LOC158056 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158056 BINDING SITE, designated SEQ ID:39716, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48940] Another function of VGAM1396 is therefore inhibition of LOC158056 (Accession XM_088463). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158056. LOC158525 (Accession XM_088593) is another VGAM1396 host target gene. LOC158525 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158525 BINDING SITE, designated SEQ ID:39859, to

the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48941] Another function of VGAM1396 is therefore inhibition of LOC158525 (Accession XM_088593). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158525. LOC197196 (Accession XM_117003) is another VGAM1396 host target gene. LOC197196 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197196 BINDING SITE, designated SEQ ID:43198, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48942] Another function of VGAM1396 is therefore inhibition of LOC197196 (Accession XM_117003). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197196. LOC221486 (Accession XM_165760) is another VGAM1396 host target gene. LOC221486 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC221486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221486 BINDING SITE, designated SEQ ID:43745, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48943] Another function of VGAM1396 is therefore inhibition of LOC221486 (Accession XM_165760). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221486. LOC51200 (Accession NM_016352) is another VGAM1396 host target gene. LOC51200 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51200, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51200 BINDING SITE, designated SEQ ID:18483, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48944] Another function of VGAM1396 is therefore inhibition of LOC51200 (Accession NM_016352). Accordingly, utilities

of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51200. LOC90381 (Accession XM_031334) is another VGAM1396 host target gene. LOC90381 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90381 BINDING SITE, designated SEQ ID:31343, to the nucleotide sequence of VGAM1396 RNA, herein designated VGAM RNA, also designated SEQ ID:4107.

[48945] Another function of VGAM1396 is therefore inhibition of LOC90381 (Accession XM_031334). Accordingly, utilities of VGAM1396 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90381. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1397 (VGAM1397) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48946] VGAM1397 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1397 was detected is described hereinabove with reference to Figs. 1–8.

[48947] VGAM1397 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cowpea Aphid–borne Mosaic Virus. VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48948] VGAM1397 gene encodes a VGAM1397 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1397 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1397 precursor RNA is designated SEQ ID:1383, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1383 is located at position 2518 relative to the genome of Cowpea Aphid–borne Mosaic Virus.

[48949] VGAM1397 precursor RNA folds onto itself, forming VGAM1397 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[48950] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1397 folded precursor RNA into VGAM1397 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 58%) nucleotide sequence of VGAM1397 RNA is designated SEQ ID:4108, and is provided hereinbelow with reference to the sequence listing part.

[48951] VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1397 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[48952] VGAM1397 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1397 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1397 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48953] The complementary binding of VGAM1397 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1397 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1397 host target RNA into VGAM1397 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48954] It is appreciated that VGAM1397 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1397 host target genes. The mRNA of each one of this plurality of VGAM1397 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1397 RNA, herein designated VGAM RNA, and which when bound by VGAM1397 RNA causes inhibition of translation of respective one or more VGAM1397 host target proteins.

[48955] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1397 gene, herein designated VGAM GENE, on one or more VGAM1397 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48956] It is yet further appreciated that a function of VGAM1397 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of viral infection by Cowpea Aphid-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1397 correlate with, and may be deduced from, the identity of the host target genes which VGAM1397 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48957] Nucleotide sequences of the VGAM1397 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1397 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1397 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1397 are further
described hereinbelow with reference to Table 1.

[48958] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1397 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1397 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[48959] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1397 gene, herein designated VGAM is
inhibition of expression of VGAM1397 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1397 correlate with, and may be deduced
from, the identity of the target genes which VGAM1397
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[48960] Diptheria Toxin Resistance Protein Required For Diph-
thamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Ac-

cession NM_001384) is a VGAM1397 host target gene. DPH2L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DPH2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPH2L2 BINDING SITE, designated SEQ ID:7057, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48961] A function of VGAM1397 is therefore inhibition of Diptheria Toxin Resistance Protein Required For Diphthamide Biosynthesis-like 2 (*S. cerevisiae*) (DPH2L2, Accession NM_001384), a gene which is required for diphthamide biosynthesis. Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPH2L2. The function of DPH2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1221. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM1397 host target gene. LRP4 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32199, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48962] Another function of VGAM1397 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_000021) is another VGAM1397 host target gene. PSEN1 BINDING SITE1 and PSEN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSEN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSEN1 BINDING SITE1 and PSEN1 BINDING SITE2, designated SEQ ID:5454 and SEQ ID:14232 respectively, to the nucleotide sequence of

VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48963] Another function of VGAM1397 is therefore inhibition of Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_000021). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSEN1. Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969) is another VGAM1397 host target gene. EIF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5 BINDING SITE, designated SEQ ID:7697, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48964] Another function of VGAM1397 is therefore inhibition of Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5. KIAA0179 (Accession XM_035973) is another VGAM1397 host target gene.

KIAA0179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0179 BINDING SITE, designated SEQ ID:32365, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48965] Another function of VGAM1397 is therefore inhibition of KIAA0179 (Accession XM_035973). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0179. KIAA0215 (Accession NM_014735) is another VGAM1397 host target gene. KIAA0215 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0215 BINDING SITE, designated SEQ ID:16382, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48966] Another function of VGAM1397 is therefore inhibition of KIAA0215 (Accession NM_014735). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0215. KIAA0459 (Accession XM_027862) is another VGAM1397 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30582, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48967] Another function of VGAM1397 is therefore inhibition of KIAA0459 (Accession XM_027862). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0459. KIAA1814 (Accession XM_046822) is another VGAM1397 host target gene. KIAA1814 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1814, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1814 BINDING SITE, designated SEQ ID:34836, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48968] Another function of VGAM1397 is therefore inhibition of KIAA1814 (Accession XM_046822). Accordingly, utilities of VGAM1397 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1814. TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256) is another VGAM1397 host target gene. TRAF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF3 BINDING SITE, designated SEQ ID:30038, to the nucleotide sequence of VGAM1397 RNA, herein designated VGAM RNA, also designated SEQ ID:4108.

[48969] Another function of VGAM1397 is therefore inhibition of TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256). Accordingly, utilities of VGAM1397 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1398 (VGAM1398) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[48970] VGAM1398 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1398 was detected is described hereinabove with reference to Figs. 1–8.

[48971] VGAM1398 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[48972] VGAM1398 gene encodes a VGAM1398 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1398 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1398 precursor RNA is desig-

nated SEQ ID:1384, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1384 is located at position 9232 relative to the genome of Perina Nuda Picorna-like Virus.

- [48973] VGAM1398 precursor RNA folds onto itself, forming VGAM1398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [48974] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1398 folded precursor RNA into VGAM1398 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1398 RNA is designated SEQ ID:4109, and is provided hereinbelow with reference to the sequence

listing part.

[48975] VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1398 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[48976] VGAM1398 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1398 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1398 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[48977] The complementary binding of VGAM1398 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1398 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1398 host target RNA into VGAM1398 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[48978] It is appreciated that VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1398 host target genes. The mRNA of each one of this plurality of VGAM1398 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1398 RNA, herein designated VGAM

RNA, and which when bound by VGAM1398 RNA causes inhibition of translation of respective one or more VGAM1398 host target proteins.

[48979] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1398 gene, herein designated VGAM GENE, on one or more VGAM1398 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[48980] It is yet further appreciated that a function of VGAM1398 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1398 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1398 correlate with, and may be deduced from, the identity of the host target genes which VGAM1398 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[48981] Nucleotide sequences of the VGAM1398 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1398 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1398 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1398 are further described hereinbelow with reference to Table 1.

[48982] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1398 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1398 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[48983] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1398 gene, herein designated VGAM is

inhibition of expression of VGAM1398 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1398 correlate with, and may be deduced from, the identity of the target genes which VGAM1398 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[48984] ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678) is a VGAM1398 host target gene. ATP1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B2 BINDING SITE, designated SEQ ID:7387, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48985] A function of VGAM1398 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678), a gene which catalyzes the hydrolysis of ATP coupled with the exchange of Na⁺/K⁺ ions across the plasma membrane. Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ATP1B2. The function of ATP1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Contactin Associated Protein-like 2 (CNTNAP2, Accession NM_014141) is another VGAM1398 host target gene. CNTNAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTNAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTNAP2 BINDING SITE, designated SEQ ID:15412, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48986] Another function of VGAM1398 is therefore inhibition of Contactin Associated Protein-like 2 (CNTNAP2, Accession NM_014141). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTNAP2. Cathepsin L (CTSL, Accession NM_001912) is another VGAM1398 host target gene. CTSL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded

by CTSL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTSL BINDING SITE, designated SEQ ID:7628, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48987] Another function of VGAM1398 is therefore inhibition of Cathepsin L (CTSL, Accession NM_001912). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTSL. GATA Binding Protein 2 (GATA2, Accession NM_002050) is another VGAM1398 host target gene. GATA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE, designated SEQ ID:7801, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48988] Another function of VGAM1398 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM_002050).

Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. Interleukin 1, Alpha (IL1A, Accession XM_031221) is another VGAM1398 host target gene. IL1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1A BINDING SITE, designated SEQ ID:31307, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48989] Another function of VGAM1398 is therefore inhibition of Interleukin 1, Alpha (IL1A, Accession XM_031221), a gene which stimulates thymocyte proliferation by inducing il-2 release, b-cell maturation & proliferation, & fibroblast growth factor activity. Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1A. The function of IL1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM475.IMP (inosine monophosphate) Dehydrogenase 1 (IMPDH1, Ac-

cession NM_000883) is another VGAM1398 host target gene. IMPDH1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IMPDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPDH1 BINDING SITE, designated SEQ ID:6577, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48990] Another function of VGAM1398 is therefore inhibition of IMP (inosine monophosphate) Dehydrogenase 1 (IMPDH1, Accession NM_000883). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPDH1. Proprotein Convertase Subtilisin/kexin Type 1 (PCSK1, Accession NM_000439) is another VGAM1398 host target gene. PCSK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCSK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCSK1 BINDING SITE, des-

ignated SEQ ID:6023, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48991] Another function of VGAM1398 is therefore inhibition of Proprotein Convertase Subtilisin/kexin Type 1 (PCSK1, Accession NM_000439), a gene which processes hormone precursors by cleaving paired basic amino acids; serine protease of the subtilase family. Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCSK1. The function of PCSK1 has been established by previous studies. A wide variety of biologically important polypeptides including hormones, enzymes, and receptors are initially synthesized as large inactive precursors. To release the active component(s), these precursors must undergo limited proteolysis at pairs of basic residues by specific convertases. There is, for example, a diarginyl-specific proalbumin convertase (see OMIM Ref. No. comment in 103600). Three mammalian convertases, PC1 (PCSK1; also known as PC3), PC2 (PCSK2; 162151), and furin (OMIM Ref. No. 136950), belonging to the family of serine proteinases of the subtilisin family, are prohormone and proprotein convertases. PC1 and PC2, known also as NEC1

and NEC2 (for neuroendocrine convertase 1 and 2, respectively), differentially cleave proopiomelanocortin (POMC; 176830). Proinsulin is converted to insulin (OMIM Ref. No. 176730) by the concerted action of PC2 and PC3. Furin is a specific proteinase capable of activating the beta subunit of pro-NGF (OMIM Ref. No. 162030) and von Willebrand factor (OMIM Ref. No. 193400). By in situ hybridization, Seidah et al. (1991) mapped NEC1 to human 5q15-q21 and to mouse chromosome 13. Copeland et al. (1992) refined the regional localization on mouse chromosome 13. Ohagi et al. (1996) stated that PC2 is responsible for cleavage of the C-peptide/A-chain junction of the proinsulin molecule, whereas PC3 cleaves the proinsulin molecule on the C-terminal side of the dibasic peptide, arg31-arg32, joining the B-chain and C-peptide. PC3 plays a key role in regulating insulin biosynthesis by initiating the sequential processing. Expression of insulin and PC3, but not PC2, is coordinately regulated by glucose, consistent with the important role of PC3 in regulating proinsulin processing. Noninsulin-dependent diabetes mellitus (NIDDM; 125853) is associated with increased secretion of proinsulin and proinsulin-like molecules, suggesting that mutations in the PC3 gene may be involved in

the development of this disorder. Ohagi et al. (1996) showed that the human PC3 gene consists of 14 exons spanning more than 35 kb. The exon/intron organization of the PC2 and PC3 genes are conserved, consistent with a common evolutionary origin. Screening for mutations in the PC3 gene in Japanese subjects with NIDDM using SSCP analysis and nucleotide sequencing of the entire coding region, Ohagi et al. (1996) could find no mutation associated with NIDDM. A mutation in carboxypeptidase E (CPE; 114855), an enzyme active in the processing and sorting of prohormones, causes obesity in the fat/fat mouse (Naggert et al., 1995; Cool et al., 1997). The gene products of CPE and PC1 cooperate in prohormone processing. Mutations in the CPE gene had not been demonstrated in human obesity. However, Jackson et al. (1997) demonstrated mutations in the prohormone convertase 1 gene, which acts proximally to CPE in the pathway of posttranslational processing of prohormones and neuropeptides. The subject was a 43-year-old woman with extreme childhood obesity, abnormal glucose homeostasis, hypogonadotropic hypogonadism, hypocortisolism, and elevated plasma proinsulin and POMC concentrations, but very low insulin levels, all suggestive of defective prohormone pro-

cessing by the patient's PC1. The patient had been described clinically by O'Rahilly et al. (1995); see 600955. The patient was found to be a compound heterozygote for mutations in PC1. Heteroallelism of the patient was confirmed by the fact that 1 substitution (162150.0001) was found in 3 of the proband's 4 children, all of whom were clinically unaffected; the fourth child had the other mutation, a splice site defect (162150.0002). The proband's fasting serum leptin (OMIM Ref. No. 164160) concentration was appropriate for her body mass index. There was a close similarity of phenotype between the proband and the fat/fat mouse.

[48992] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[48993] Ohagi, S.; Sakaguchi, H.; Sanke, T.; Tatsuta, H.; Hanabusa, T.; Nanjo, K. : Human prohormone convertase 3 gene: exon-intron organization and molecular scanning for mutations in Japanese subjects with NIDDM. Diabetes 45: 897-901, 1996. ; and

[48994] O'Rahilly, S.; Gray, H.; Humphreys, P. J.; Krook, A.; Polonsky, K. S.; White, A.; Gibson, S.; Taylor, K.; Carr, C. : Brief report: impaired processing of prohormones associated

with abno.

[48995] Further studies establishing the function and utilities of PCSK1 are found in John Hopkins OMIM database record ID 162150, and in cited publications numbered 1712, 3577–195 and 3583 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BICD2 (Accession XM_046863) is another VGAM1398 host target gene. BICD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BICD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BICD2 BINDING SITE, designated SEQ ID:34851, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48996] Another function of VGAM1398 is therefore inhibition of BICD2 (Accession XM_046863). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BICD2. FLJ31709 (Accession NM_144636) is another VGAM1398 host target gene. FLJ31709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ31709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31709 BINDING SITE, designated SEQ ID:29456, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48997] Another function of VGAM1398 is therefore inhibition of FLJ31709 (Accession NM_144636). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31709. KIAA0285 (Accession NM_014807) is another VGAM1398 host target gene. KIAA0285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0285 BINDING SITE, designated SEQ ID:16745, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48998] Another function of VGAM1398 is therefore inhibition of KIAA0285 (Accession NM_014807). Accordingly, utilities

of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0285. KIAA0367 (Accession XM_041018) is another VGAM1398 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33423, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[48999] Another function of VGAM1398 is therefore inhibition of KIAA0367 (Accession XM_041018). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA1649 (Accession NM_032311) is another VGAM1398 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1649 BINDING SITE, designated SEQ ID:26114, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49000] Another function of VGAM1398 is therefore inhibition of KIAA1649 (Accession NM_032311). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. MGC2306 (Accession NM_032638) is another VGAM1398 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26350, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49001] Another function of VGAM1398 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. POMT2 (Accession NM_013382) is another VGAM1398 host target gene. POMT2 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by POMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMT2 BINDING SITE, designated SEQ ID:15034, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49002] Another function of VGAM1398 is therefore inhibition of POMT2 (Accession NM_013382). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMT2. PRO2032 (Accession NM_018615) is another VGAM1398 host target gene. PRO2032 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2032 BINDING SITE, designated SEQ ID:20684, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49003] Another function of VGAM1398 is therefore inhibition of

PRO2032 (Accession NM_018615). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2032. RAB20, Member RAS Oncogene Family (RAB20, Accession NM_017817) is another VGAM1398 host target gene. RAB20 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RAB20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB20 BINDING SITE, designated SEQ ID:19464, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49004] Another function of VGAM1398 is therefore inhibition of RAB20, Member RAS Oncogene Family (RAB20, Accession NM_017817). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB20. Tumor Protein D52 (TPD52, Accession NM_005079) is another VGAM1398 host target gene. TPD52 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TPD52, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPD52 BINDING SITE, designated SEQ ID:11531, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49005] Another function of VGAM1398 is therefore inhibition of Tumor Protein D52 (TPD52, Accession NM_005079). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPD52. LOC115399 (Accession XM_055874) is another VGAM1398 host target gene. LOC115399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115399 BINDING SITE, designated SEQ ID:36344, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49006] Another function of VGAM1398 is therefore inhibition of LOC115399 (Accession XM_055874). Accordingly, utilities

of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115399. LOC146243 (Accession XM_096956) is another VGAM1398 host target gene. LOC146243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146243 BINDING SITE, designated SEQ ID:40674, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49007] Another function of VGAM1398 is therefore inhibition of LOC146243 (Accession XM_096956). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146243. LOC148293 (Accession XM_086138) is another VGAM1398 host target gene. LOC148293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC148293 BINDING SITE, designated SEQ ID:38517, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49008] Another function of VGAM1398 is therefore inhibition of LOC148293 (Accession XM_086138). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148293. LOC256073 (Accession XM_172972) is another VGAM1398 host target gene. LOC256073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256073 BINDING SITE, designated SEQ ID:46227, to the nucleotide sequence of VGAM1398 RNA, herein designated VGAM RNA, also designated SEQ ID:4109.

[49009] Another function of VGAM1398 is therefore inhibition of LOC256073 (Accession XM_172972). Accordingly, utilities of VGAM1398 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256073. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1399 (VGAM1399) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49010] VGAM1399 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1399 was detected is described hereinabove with reference to Figs. 1–8.

[49011] VGAM1399 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49012] VGAM1399 gene encodes a VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1399 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1399 precursor RNA is designated SEQ ID:1385, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1385 is located at position 2981 relative to the

genome of Perina Nuda Picorna-like Virus.

[49013] VGAM1399 precursor RNA folds onto itself, forming VGAM1399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49014] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1399 folded precursor RNA into VGAM1399 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1399 RNA is designated SEQ ID:4110, and is provided hereinbelow with reference to the sequence listing part.

[49015] VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1399 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[49016] VGAM1399 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1399 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1399 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49017] The complementary binding of VGAM1399 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1399 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1399 host target RNA into VGAM1399 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49018] It is appreciated that VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1399 host target genes. The mRNA of each one of this plurality of VGAM1399 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1399 RNA, herein designated VGAM RNA, and which when bound by VGAM1399 RNA causes inhibition of translation of respective one or more VGAM1399 host target proteins.

[49019] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1399 gene, herein designated VGAM GENE, on one or more VGAM1399 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49020] It is yet further appreciated that a function of VGAM1399 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of

VGAM1399 correlate with, and may be deduced from, the identity of the host target genes which VGAM1399 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49021] Nucleotide sequences of the VGAM1399 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1399 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1399 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1399 are further described hereinbelow with reference to Table 1.

[49022] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1399 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1399 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49023] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1399 gene, herein designated VGAM is inhibition of expression of VGAM1399 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1399 correlate with, and may be deduced

from, the identity of the target genes which VGAM1399 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49024] Membrane Protein, Palmitoylated 6 (MAGUK p55 subfamily member 6) (MPP6, Accession NM_016447) is a VGAM1399 host target gene. MPP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MPP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP6 BINDING SITE, designated SEQ ID:18566, to the nucleotide sequence of VGAM1399 RNA, herein designated VGAM RNA, also designated SEQ ID:4110.

[49025] A function of VGAM1399 is therefore inhibition of Membrane Protein, Palmitoylated 6 (MAGUK p55 subfamily member 6) (MPP6, Accession NM_016447), a gene which may regulate transmembrane proteins that bind calcium, calmodulin, or nucleotides. Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP6. The function of MPP6 has been established by previous studies. By searching an EST database with DLG2 (OMIM

Ref. No. 603583) as the probe, followed by PCR of a brain cDNA library and 5-prime RACE, Tseng et al. (2001) obtained a cDNA encoding MPP6, which they called VAM1 for VELI (OMIM Ref. No. 603380)-associated MAGUK-1. The deduced 540-amino acid protein has a single PDZ domain, a central SH3 domain, and a C-terminal GUK domain, resembling other members of the p55 MAGUK subfamily. Like MPP1, MPP6 also contains a protein 4.1 (EPB41; 130500)-binding domain with its characteristic KKKK sequence, as well as a leucine zipper and 2 phosphorylation sites. Northern blot analysis revealed expression of an abundant 2.3-kb transcript and a minor 4.2-kb transcript only in testis. RT-PCR analysis detected predominant expression in testis, with lower amounts in ovary, prostate, thymus, small intestine, and several other tissues; VELI has a similar expression pattern. GST pull-down and mutation analyses indicated that a domain N-terminal of the PDZ region of VAM1 contains the minimal VELI-binding sequence. No binding between VAM1 and EPB41 was detected. Kamberov et al. (2000) cloned and characterized the mouse Mpp5 (OMIM Ref. No. 606958) and Mpp6 genes, which they called Pals1 and Pals2, respectively. The Pals proteins bind to mouse Lin7 (VELI)

through a region N-terminal to their PDZ domains.

[49026] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49027] Kamberov, E.; Makarova, O.; Roh, M.; Liu, A.; Karnak, D.; Straight, S.; Margolis, B. : Molecular cloning and characterization of Pals, proteins associated with mLin-7. J. Biol. Chem. 275: 11425-11431, 2000. ; and

[49028] Tseng, T.-C.; Marfatia, S. M.; Bryant, P. J.; Pack, S.; Zhuang, A.; O'Brien, J. E.; Lin, L.; Hanada, T.; Chishti, A. H. : VAM-1: a new member of the MAGUK family binds to human Veli-1.

[49029] Further studies establishing the function and utilities of MPP6 are found in John Hopkins OMIM database record ID 606959, and in cited publications numbered 5138-5139 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10326 (Accession NM_018060) is another VGAM1399 host target gene. FLJ10326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ10326 BINDING SITE, designated SEQ ID:19829, to the nucleotide sequence of VGAM1399 RNA, herein designated VGAM RNA, also designated SEQ ID:4110.

[49030] Another function of VGAM1399 is therefore inhibition of FLJ10326 (Accession NM_018060). Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10326. KIAA1111 (Accession XM_171233) is another VGAM1399 host target gene. KIAA1111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1111 BINDING SITE, designated SEQ ID:46018, to the nucleotide sequence of VGAM1399 RNA, herein designated VGAM RNA, also designated SEQ ID:4110.

[49031] Another function of VGAM1399 is therefore inhibition of KIAA1111 (Accession XM_171233). Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1111. MGC32104 (Accession NM_144684) is another

VGAM1399 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29507, to the nucleotide sequence of VGAM1399 RNA, herein designated VGAM RNA, also designated SEQ ID:4110.

[49032] Another function of VGAM1399 is therefore inhibition of MGC32104 (Accession NM_144684). Accordingly, utilities of VGAM1399 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1400 (VGAM1400) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49033] VGAM1400 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1400 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[49034] VGAM1400 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna–like Virus. VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49035] VGAM1400 gene encodes a VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1400 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1400 precursor RNA is designated SEQ ID:1386, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1386 is located at position 2576 relative to the genome of Perina Nuda Picorna–like Virus.

[49036] VGAM1400 precursor RNA folds onto itself, forming VGAM1400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49037] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1400 folded precursor RNA into VGAM1400 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1400 RNA is designated SEQ ID:4111, and is provided hereinbelow with reference to the sequence listing part.

[49038] VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1400 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49039] VGAM1400 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1400 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1400 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1400 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49040] The complementary binding of VGAM1400 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1400 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1400 host target RNA into VGAM1400 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49041] It is appreciated that VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1400 host target genes. The mRNA of each one of this plurality of VGAM1400 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1400 RNA, herein designated VGAM RNA, and which when bound by VGAM1400 RNA causes inhibition of translation of respective one or more VGAM1400 host target proteins.

[49042] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1400 gene, herein designated VGAM GENE, on one or more VGAM1400 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49043] It is yet further appreciated that a function of VGAM1400 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1400 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1400 correlate with, and may be deduced from, the identity of the host target genes which VGAM1400 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49044] Nucleotide sequences of the VGAM1400 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1400 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1400 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1400 are further described hereinbelow with reference to Table 1.

[49045] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1400 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1400 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49046] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1400 gene, herein designated VGAM is inhibition of expression of VGAM1400 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1400 correlate with, and may be deduced from, the identity of the target genes which VGAM1400 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49047] KIAA0379 (Accession XM_042860) is a VGAM1400 host target gene. KIAA0379 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0379, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0379 BINDING SITE, designated SEQ ID:33811, to the nucleotide sequence of VGAM1400 RNA, herein designated VGAM RNA, also designated SEQ ID:4111.

[49048] A function of VGAM1400 is therefore inhibition of KIAA0379 (Accession XM_042860). Accordingly, utilities of VGAM1400 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0379. KIAA1610 (Accession XM_040622) is another VGAM1400 host target gene. KIAA1610 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1610 BINDING SITE, designated SEQ ID:33340, to the nucleotide sequence of VGAM1400 RNA, herein designated VGAM RNA, also designated SEQ ID:4111.

[49049] Another function of VGAM1400 is therefore inhibition of KIAA1610 (Accession XM_040622). Accordingly, utilities of VGAM1400 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1610. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1401 (VGAM1401) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49050] VGAM1401 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1401 was detected is described hereinabove with reference to Figs. 1–8.

[49051] VGAM1401 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49052] VGAM1401 gene encodes a VGAM1401 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1401 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1401 precursor RNA is designated SEQ ID:1387, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1387 is located at position 7823 relative to the genome of Perina Nuda Picorna-like Virus.

[49053] VGAM1401 precursor RNA folds onto itself, forming VGAM1401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49054] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1401 folded precursor RNA into VGAM1401 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1401 RNA is designated SEQ ID:4112, and is provided hereinbelow with reference to the sequence listing part.

[49055] VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1401 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49056] VGAM1401 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1401 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1401 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49057] The complementary binding of VGAM1401 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1401 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1401 host target RNA into VGAM1401 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49058] It is appreciated that VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1401 host target genes. The mRNA of each one of this plurality of VGAM1401 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1401 RNA, herein designated VGAM RNA, and which when bound by VGAM1401 RNA causes

inhibition of translation of respective one or more VGAM1401 host target proteins.

[49059] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1401 gene, herein designated VGAM GENE, on one or more VGAM1401 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49060] It is yet further appreciated that a function of VGAM1401 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1401 include diagnosis, prevention and

treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1401 correlate with, and may be deduced from, the identity of the host target genes which VGAM1401 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49061] Nucleotide sequences of the VGAM1401 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1401 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1401 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1401 are further described hereinbelow with reference to Table 1.

[49062] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1401 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1401 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49063] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1401 gene, herein designated VGAM is inhibition of expression of VGAM1401 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1401 correlate with, and may be deduced from, the identity of the target genes which VGAM1401 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49064] Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530) is a VGAM1401 host target gene. HIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIF1A BINDING SITE, designated SEQ ID:7269, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49065] A function of VGAM1401 is therefore inhibition of Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530), a gene which is a basic helix-loop-helix transcription factor and mediates transcriptional responses to hypoxia and dioxin-signaling. Accordingly, utilities of VGAM1401 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with HIF1A. The function of HIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 2 (KCNS2, Accession XM_043106) is another VGAM1401 host target gene. KCNS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS2 BINDING SITE, designated SEQ ID:33897, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49066] Another function of VGAM1401 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 2 (KCNS2, Accession XM_043106), a gene which mediates the voltage-dependent potassium ion permeability of excitable membranes. Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with KCNS2. The function of KCNS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM419. RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM_014781) is another VGAM1401 host target gene. RB1CC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RB1CC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RB1CC1 BINDING SITE, designated SEQ ID:16632, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49067] Another function of VGAM1401 is therefore inhibition of RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM_014781), a gene which is likely to participate in nuclear architecture by connecting chromatin with the nuclear matrix or envelope. Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RB1CC1. The function of RB1CC1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM18. Sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, fungal)-like (SC5DL, Accession XM_165583) is another VGAM1401 host target gene.

SC5DL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SC5DL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SC5DL BINDING SITE, designated SEQ ID:43697, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49068] Another function of VGAM1401 is therefore inhibition of Sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, fungal)-like (SC5DL, Accession XM_165583). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SC5DL. Secreted Frizzled-related Protein 4 (SFRP4, Accession NM_003014) is another VGAM1401 host target gene. SFRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRP4, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP4 BINDING SITE, designated SEQ ID:8939, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49069] Another function of VGAM1401 is therefore inhibition of Secreted Frizzled-related Protein 4 (SFRP4, Accession NM_003014). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP4. Short Stature Homeobox (SHOX, Accession NM_000451) is another VGAM1401 host target gene. SHOX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHOX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHOX BINDING SITE, designated SEQ ID:6057, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49070] Another function of VGAM1401 is therefore inhibition of Short Stature Homeobox (SHOX, Accession NM_000451).

Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHOX. SudD Suppressor of BimD6 Homolog (*A. nidulans*) (SUDD, Accession NM_003831) is another VGAM1401 host target gene. SUDD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUDD BINDING SITE, designated SEQ ID:9923, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49071] Another function of VGAM1401 is therefore inhibition of SudD Suppressor of BimD6 Homolog (*A. nidulans*) (SUDD, Accession NM_003831). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUDD. SUV39H2 (Accession NM_024670) is another VGAM1401 host target gene. SUV39H2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUV39H2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUV39H2 BINDING SITE, designated SEQ ID:23976, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49072] Another function of VGAM1401 is therefore inhibition of SUV39H2 (Accession NM_024670), a gene which is involved in gene repression and the modification of position-effect-variegation. Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUV39H2. The function of SUV39H2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM424. Ubiquitin-like 3 (UBL3, Accession NM_007106) is another VGAM1401 host target gene. UBL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBL3 BINDING SITE, designated SEQ ID:13967, to the nucleotide sequence of VGAM1401 RNA, herein

designated VGAM RNA, also designated SEQ ID:4112.

[49073] Another function of VGAM1401 is therefore inhibition of Ubiquitin-like 3 (UBL3, Accession NM_007106), a gene which appears to have a diverse range of cellular functions. Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBL3. The function of UBL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM459.FLJ23074 (Accession NM_025052) is another VGAM1401 host target gene. FLJ23074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23074 BINDING SITE, designated SEQ ID:24650, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49074] Another function of VGAM1401 is therefore inhibition of FLJ23074 (Accession NM_025052). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ23074. SFRS Protein Kinase 1 (SRPK1, Accession NM_003137) is another VGAM1401 host target gene. SRPK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SRPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRPK1 BINDING SITE, designated SEQ ID:9107, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49075] Another function of VGAM1401 is therefore inhibition of SFRS Protein Kinase 1 (SRPK1, Accession NM_003137). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRPK1. LOC158130 (Accession XM_044880) is another VGAM1401 host target gene. LOC158130 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158130 BINDING SITE, desig-

nated SEQ ID:34302, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49076] Another function of VGAM1401 is therefore inhibition of LOC158130 (Accession XM_044880). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158130. LOC202781 (Accession XM_117455) is another VGAM1401 host target gene. LOC202781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202781 BINDING SITE, designated SEQ ID:43442, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49077] Another function of VGAM1401 is therefore inhibition of LOC202781 (Accession XM_117455). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202781. LOC221962 (Accession XM_166554) is another VGAM1401 host target gene. LOC221962 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221962 BINDING SITE, designated SEQ ID:44530, to the nucleotide sequence of VGAM1401 RNA, herein designated VGAM RNA, also designated SEQ ID:4112.

[49078] Another function of VGAM1401 is therefore inhibition of LOC221962 (Accession XM_166554). Accordingly, utilities of VGAM1401 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221962. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1402 (VGAM1402) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49079] VGAM1402 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1402 was detected is described hereinabove with reference to Figs. 1-8.

[49080] VGAM1402 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49081] VGAM1402 gene encodes a VGAM1402 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1402 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1402 precursor RNA is designated SEQ ID:1388, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1388 is located at position 7345 relative to the genome of Perina Nuda Picorna-like Virus.

[49082] VGAM1402 precursor RNA folds onto itself, forming VGAM1402 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[49083] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1402 folded precursor RNA into VGAM1402 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1402 RNA is designated SEQ ID:4113, and is provided hereinbelow with reference to the sequence listing part.

[49084] VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1402 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49085] VGAM1402 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1402 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1402 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1402 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49086] The complementary binding of VGAM1402 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1402 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1402 host target RNA into VGAM1402 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49087] It is appreciated that VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1402 host target genes. The mRNA of each one of this plurality of VGAM1402 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1402 RNA, herein designated VGAM RNA, and which when bound by VGAM1402 RNA causes inhibition of translation of respective one or more VGAM1402 host target proteins.

[49088] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1402 gene, herein designated VGAM GENE, on one or more VGAM1402 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49089] It is yet further appreciated that a function of VGAM1402 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1402 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1402 correlate with, and may be deduced from, the identity of the host target genes which VGAM1402 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49090] Nucleotide sequences of the VGAM1402 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1402 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1402 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1402 are further described hereinbelow with reference to Table 1.

[49091] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1402 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1402 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49092] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1402 gene, herein designated VGAM is inhibition of expression of VGAM1402 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1402 correlate with, and may be deduced from, the identity of the target genes which VGAM1402 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49093] LOC90342 (Accession XM_031009) is a VGAM1402 host target gene. LOC90342 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC90342 BINDING SITE, designated SEQ ID:31248, to the nucleotide sequence of VGAM1402 RNA, herein designated VGAM RNA, also designated SEQ ID:4113.

[49094] A function of VGAM1402 is therefore inhibition of LOC90342 (Accession XM_031009). Accordingly, utilities of VGAM1402 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90342. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1403 (VGAM1403) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49095] VGAM1403 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1403 was detected is described hereinabove with reference to Figs. 1–8.

[49096] VGAM1403 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[49097] VGAM1403 gene encodes a VGAM1403 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1403 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1403 precursor RNA is designated SEQ ID:1389, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1389 is located at position 7194 relative to the genome of Perina Nuda Picorna-like Virus.

[49098] VGAM1403 precursor RNA folds onto itself, forming VGAM1403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49099] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1403 folded precursor RNA into VGAM1403 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1403 RNA is designated SEQ ID:4114, and is provided hereinbelow with reference to the sequence listing part.

[49100] VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1403 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49101] VGAM1403 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1403 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1403 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49102] The complementary binding of VGAM1403 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1403 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1403 host target RNA into VGAM1403 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49103] It is appreciated that VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1403 host target genes. The mRNA of each one of this plurality of VGAM1403 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1403 RNA, herein designated VGAM RNA, and which when bound by VGAM1403 RNA causes inhibition of translation of respective one or more VGAM1403 host target proteins.

[49104] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1403 gene, herein designated VGAM GENE, on one or more VGAM1403 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49105] It is yet further appreciated that a function of VGAM1403 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1403 correlate with, and may be deduced from, the identity of the host target genes which VGAM1403 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49106] Nucleotide sequences of the VGAM1403 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1403 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1403 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1403 are further described hereinbelow with reference to Table 1.

[49107] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1403 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1403 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49108] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1403 gene, herein designated VGAM is inhibition of expression of VGAM1403 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1403 correlate with, and may be deduced from, the identity of the target genes which VGAM1403 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49109] Amyotrophic Lateral Sclerosis 2 (juvenile) (ALS2, Accession NM_020919) is a VGAM1403 host target gene. ALS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2 BINDING SITE, designated SEQ ID:21928, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49110] A function of VGAM1403 is therefore inhibition of Amyotrophic Lateral Sclerosis 2 (juvenile) (ALS2, Accession NM_020919). Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALS2. Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286) is another VGAM1403 host target gene. AQP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP6 BINDING SITE, designated SEQ ID:27611, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49111] Another function of VGAM1403 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286), a gene which participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism. Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 and its association with vari-

ous diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1, Accession NM_004360) is another VGAM1403 host target gene. CDH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH1 BINDING SITE, designated SEQ ID:10563, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49112] Another function of VGAM1403 is therefore inhibition of Cadherin 1, Type 1, E-cadherin (epithelial) (CDH1, Accession NM_004360). Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH1. Cytochrome P450, Subfamily VIIB (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391) is another VGAM1403 host target gene. CYP8B1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYP8B1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP8B1 BINDING SITE, designated SEQ ID:10623, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49113] Another function of VGAM1403 is therefore inhibition of Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391), a gene which functions in bile acid biosynthesis. Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP8B1. The function of CYP8B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. Eukaryotic Translation Initiation Factor 4 Gamma, 1 (EIF4G1, Accession NM_004953) is another VGAM1403 host target gene. EIF4G1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EIF4G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of EIF4G1 BINDING SITE, designated SEQ ID:11396, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49114] Another function of VGAM1403 is therefore inhibition of Eukaryotic Translation Initiation Factor 4 Gamma, 1 (EIF4G1, Accession NM_004953), a gene which is a Translation initiation factor. Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4G1. The function of EIF4G1 has been established by previous studies. Gradi et al. (1998) identified a second human eIF4G gene. They designated the original gene eIF4GI and the novel gene eIF4GII (EIF4G3; 603929). Imataka et al. (1998) found that the human eIF4GI protein contains an additional 156 N-terminal amino acids compared to the sequence published by Yan et al. (1992). They demonstrated that this N-terminal region binds poly(A)-binding protein (PABP; 604679). In an in vitro translation system, an N-terminal fragment of eIF4GI that included the PABP-binding site inhibited poly(A)-dependent translation, but had no effect on translation of a deadenylated mRNA. Imataka et al. (1998) concluded that eIF4G probably func-

tions in poly(A)–dependent translation in mammalian cells. By screening a rabbit brain library with oligonucleotide probes based on the sequence of rabbit eIF4–gamma peptides, Yan et al. (1992) identified partial eIF4–gamma cDNAs. They used the rabbit cDNAs as probes and isolated human brain cDNAs encoding eIF4–gamma. The predicted human protein contains 1,396 amino acids. Western blot analysis of poliovirus–infected HeLa cell extracts revealed that eIF4–gamma has an apparent molecular weight of 200 to 220 kD and is cleaved by this picornavirus. Imataka and Sonenberg (1997) stated that the N–terminal region of eIF4G contains a binding site for eIF4E. They demonstrated that the central third of eIF4G contains an eIF3 (see OMIM Ref. No. 602039)–binding region and an eIF4A–binding domain. A second, separate eIF4A–binding site is present in the C–terminal third. Neither eIF4A–binding domain alone activates translation. In contrast to eIF4G, the eIF4G–related translation regulator p97 (OMIM Ref. No. 602325) binds eIF4A only through its N–terminal domain, which is homologous to the central domain of eIF4G

[49115] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [49116] Imataka, H.; Gradi, A.; Sonenberg, N. : A newly identified N-terminal amino acid sequence of human eIF4G binds poly(A)-binding protein and functions in poly(A)-dependent translation. EMBO J. 17: 7480-7489, 1998. ; and
- [49117] Imataka, H.; Sonenberg, N. : Human eukaryotic translation initiation factor 4G (eIF4G) possesses two separate and independent binding sites for eIF4A. Molec. Cell. Biol. 17: 6940-6947.
- [49118] Further studies establishing the function and utilities of EIF4G1 are found in John Hopkins OMIM database record ID 600495, and in cited publications numbered 10197-10200, 821 and 10201-10202 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM_005628) is another VGAM1403 host target gene. SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SLC1A5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the comple-

mentarity of the nucleotide sequences of SLC1A5 BINDING SITE1 and SLC1A5 BINDING SITE2, designated SEQ ID:12141 and SEQ ID:38401 respectively, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49119] Another function of VGAM1403 is therefore inhibition of Solute Carrier Family 1 (neutral amino acid transporter), Member 5 (SLC1A5, Accession NM_005628). Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A5. FLJ20033 (Accession NM_017629) is another VGAM1403 host target gene. FLJ20033 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20033, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20033 BINDING SITE, designated SEQ ID:19126, to the nucleotide sequence of VGAM1403 RNA, herein designated VGAM RNA, also designated SEQ ID:4114.

[49120] Another function of VGAM1403 is therefore inhibition of FLJ20033 (Accession NM_017629). Accordingly, utilities of VGAM1403 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20033. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1404 (VGAM1404) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49121] VGAM1404 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1404 was detected is described hereinabove with reference to Figs. 1–8.

[49122] VGAM1404 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49123] VGAM1404 gene encodes a VGAM1404 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1404 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1404 precursor RNA is desig-

nated SEQ ID:1390, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1390 is located at position 8964 relative to the genome of Perina Nuda Picorna-like Virus.

- [49124] VGAM1404 precursor RNA folds onto itself, forming VGAM1404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49125] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1404 folded precursor RNA into VGAM1404 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM1404 RNA is designated SEQ ID:4115, and is provided hereinbelow with reference to the sequence

listing part.

[49126] VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1404 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49127] VGAM1404 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1404 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1404 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49128] The complementary binding of VGAM1404 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1404 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1404 host target RNA into VGAM1404 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49129] It is appreciated that VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1404 host target genes. The mRNA of each one of this plurality of VGAM1404 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1404 RNA, herein designated VGAM

RNA, and which when bound by VGAM1404 RNA causes inhibition of translation of respective one or more VGAM1404 host target proteins.

[49130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1404 gene, herein designated VGAM GENE, on one or more VGAM1404 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49131] It is yet further appreciated that a function of VGAM1404 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1404 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1404 correlate with, and may be deduced from, the identity of the host target genes which VGAM1404 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49132] Nucleotide sequences of the VGAM1404 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1404 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1404 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1404 are further described hereinbelow with reference to Table 1.

[49133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1404 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1404 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49134] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1404 gene, herein designated VGAM is

inhibition of expression of VGAM1404 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1404 correlate with, and may be deduced from, the identity of the target genes which VGAM1404 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49135] Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM_001649) is a VGAM1404 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7355, to the nucleotide sequence of VGAM1404 RNA, herein designated VGAM RNA, also designated SEQ ID:4115.

[49136] A function of VGAM1404 is therefore inhibition of Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM1404 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. KIAA0193 (Accession NM_014766) is another VGAM1404 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16546, to the nucleotide sequence of VGAM1404 RNA, herein designated VGAM RNA, also designated SEQ ID:4115.

[49137] Another function of VGAM1404 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities of VGAM1404 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. LOC151414 (Accession XM_087197) is another VGAM1404 host target gene. LOC151414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC151414 BINDING SITE, designated SEQ ID:39112, to the nucleotide sequence of VGAM1404 RNA, herein designated VGAM RNA, also designated SEQ ID:4115.

[49138] Another function of VGAM1404 is therefore inhibition of LOC151414 (Accession XM_087197). Accordingly, utilities of VGAM1404 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151414. LOC254532 (Accession XM_172961) is another VGAM1404 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46213, to the nucleotide sequence of VGAM1404 RNA, herein designated VGAM RNA, also designated SEQ ID:4115.

[49139] Another function of VGAM1404 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM1404 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1405 (VGAM1405) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49140] VGAM1405 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1405 was detected is described hereinabove with reference to Figs. 1–8.

[49141] VGAM1405 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49142] VGAM1405 gene encodes a VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1405 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1405 precursor RNA is designated SEQ ID:1391, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1391 is located at position 3355 relative to the

genome of Perina Nuda Picorna-like Virus.

[49143] VGAM1405 precursor RNA folds onto itself, forming VGAM1405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49144] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1405 folded precursor RNA into VGAM1405 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM1405 RNA is designated SEQ ID:4116, and is provided hereinbelow with reference to the sequence listing part.

[49145] VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1405 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49146] VGAM1405 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1405 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1405 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49147] The complementary binding of VGAM1405 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1405 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1405 host target RNA into VGAM1405 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49148] It is appreciated that VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1405 host target genes. The mRNA of each one of this plurality of VGAM1405 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1405 RNA, herein designated VGAM RNA, and which when bound by VGAM1405 RNA causes inhibition of translation of respective one or more VGAM1405 host target proteins.

[49149] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1405 gene, herein designated VGAM GENE, on one or more VGAM1405 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49150] It is yet further appreciated that a function of VGAM1405 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of

VGAM1405 correlate with, and may be deduced from, the identity of the host target genes which VGAM1405 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49151] Nucleotide sequences of the VGAM1405 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1405 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1405 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1405 are further described hereinbelow with reference to Table 1.

[49152] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1405 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1405 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49153] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1405 gene, herein designated VGAM is inhibition of expression of VGAM1405 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1405 correlate with, and may be deduced

from, the identity of the target genes which VGAM1405 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49154] Frizzled Homolog 10 (Drosophila) (FZD10, Accession NM_007197) is a VGAM1405 host target gene. FZD10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD10 BINDING SITE, designated SEQ ID:14053, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49155] A function of VGAM1405 is therefore inhibition of Frizzled Homolog 10 (Drosophila) (FZD10, Accession NM_007197). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD10. Mitogen-activated Protein Kinase 4 (MAPK4, Accession NM_002747) is another VGAM1405 host target gene. MAPK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK4 BINDING SITE, designated SEQ ID:8619, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49156] Another function of VGAM1405 is therefore inhibition of Mitogen-activated Protein Kinase 4 (MAPK4, Accession NM_002747), a gene which phosphorylates microtubule-associated protein-2 may promote entry into the cell cycle. Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK4. The function of MAPK4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM655. TIA1 Cytotoxic Granule-associated RNA Binding Protein (TIA1, Accession NM_022037) is another VGAM1405 host target gene. TIA1 BINDING SITE1 and TIA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TIA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIA1 BINDING SITE1 and

TIA1 BINDING SITE2, designated SEQ ID:22558 and SEQ ID:22733 respectively, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49157] Another function of VGAM1405 is therefore inhibition of TIA1 Cytotoxic Granule-associated RNA Binding Protein (TIA1, Accession NM_022037), a gene which possesses nucleolytic activity against cytotoxic lymphocyte target cells. Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIA1. The function of TIA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. Zinc Finger Protein 216 (ZNF216, Accession NM_006007) is another VGAM1405 host target gene. ZNF216 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF216 BINDING SITE, designated SEQ ID:12619, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM

RNA, also designated SEQ ID:4116.

[49158] Another function of VGAM1405 is therefore inhibition of Zinc Finger Protein 216 (ZNF216, Accession NM_006007). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF216. DKFZP566M114 (Accession NM_032128) is another VGAM1405 host target gene. DKFZP566M114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566M114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566M114 BINDING SITE, designated SEQ ID:25815, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49159] Another function of VGAM1405 is therefore inhibition of DKFZP566M114 (Accession NM_032128). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566M114. EFA6R (Accession NM_015310) is another VGAM1405 host target gene. EFA6R BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by EFA6R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFA6R BINDING SITE, designated SEQ ID:17622, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49160] Another function of VGAM1405 is therefore inhibition of EFA6R (Accession NM_015310). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFA6R. FLJ23816 (Accession NM_144655) is another VGAM1405 host target gene. FLJ23816 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23816 BINDING SITE, designated SEQ ID:29477, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49161] Another function of VGAM1405 is therefore inhibition of FLJ23816 (Accession NM_144655). Accordingly, utilities of

VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23816. KIAA0478 (Accession NM_014870) is another VGAM1405 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16991, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49162] Another function of VGAM1405 is therefore inhibition of KIAA0478 (Accession NM_014870). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0478. KIAA1871 (Accession XM_028409) is another VGAM1405 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1871 BINDING SITE, designated SEQ ID:30701, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49163] Another function of VGAM1405 is therefore inhibition of KIAA1871 (Accession XM_028409). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. MGC22014 (Accession XM_035307) is another VGAM1405 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32214, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49164] Another function of VGAM1405 is therefore inhibition of MGC22014 (Accession XM_035307). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22014. Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531) is another VGAM1405 host target

gene. PRKWNK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRKWNK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKWNK2 BINDING SITE, designated SEQ ID:43516, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49165] Another function of VGAM1405 is therefore inhibition of Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKWNK2. Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842) is another VGAM1405 host target gene. SPRY2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SPRY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPRY2 BINDING SITE, designated SEQ ID:12455, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA,

also designated SEQ ID:4116.

[49166] Another function of VGAM1405 is therefore inhibition of Sprouty Homolog 2 (Drosophila) (SPRY2, Accession NM_005842). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPRY2. LOC122786 (Accession XM_058660) is another VGAM1405 host target gene. LOC122786 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122786 BINDING SITE, designated SEQ ID:36701, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49167] Another function of VGAM1405 is therefore inhibition of LOC122786 (Accession XM_058660). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122786. LOC203275 (Accession XM_114667) is another VGAM1405 host target gene. LOC203275 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC203275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203275 BINDING SITE, designated SEQ ID:43026, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49168] Another function of VGAM1405 is therefore inhibition of LOC203275 (Accession XM_114667). Accordingly, utilities of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203275. LOC257319 (Accession XM_171049) is another VGAM1405 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45828, to the nucleotide sequence of VGAM1405 RNA, herein designated VGAM RNA, also designated SEQ ID:4116.

[49169] Another function of VGAM1405 is therefore inhibition of LOC257319 (Accession XM_171049). Accordingly, utilities

of VGAM1405 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1406 (VGAM1406) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49170] VGAM1406 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1406 was detected is described hereinabove with reference to Figs. 1-8.

[49171] VGAM1406 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Perina Nuda Picorna-like Virus. VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49172] VGAM1406 gene encodes a VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1406 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1406 precursor RNA is designated SEQ ID:1392, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1392 is located at position 6999 relative to the genome of Perina Nuda Picorna-like Virus.

- [49173] VGAM1406 precursor RNA folds onto itself, forming VGAM1406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49174] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1406 folded precursor RNA into VGAM1406 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1406 RNA is designated SEQ ID:4117, and

is provided hereinbelow with reference to the sequence listing part.

[49175] VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1406 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49176] VGAM1406 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1406 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1406 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49177] The complementary binding of VGAM1406 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1406 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1406 host target RNA into VGAM1406 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49178] It is appreciated that VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1406 host target genes. The mRNA of each one of this plurality of VGAM1406 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1406 RNA, herein designated VGAM RNA, and which when bound by VGAM1406 RNA causes inhibition of translation of respective one or more VGAM1406 host target proteins.

[49179] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1406 gene, herein designated VGAM GENE, on one or more VGAM1406 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49180] It is yet further appreciated that a function of VGAM1406 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1406 include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGAM1406 correlate with, and may be deduced from, the identity of the host target genes which VGAM1406 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49181] Nucleotide sequences of the VGAM1406 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1406 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1406 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1406 are further described hereinbelow with reference to Table 1.

[49182] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1406 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1406 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49183] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1406 gene, herein designated VGAM is inhibition of expression of VGAM1406 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1406 correlate with, and may be deduced from, the identity of the target genes which VGAM1406 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49184] DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Accession NM_001356) is a VGAM1406 host target gene. DDX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX3 BINDING SITE, designated SEQ ID:7032, to the nucleotide sequence of VGAM1406 RNA, herein designated VGAM RNA, also designated SEQ ID:4117.

[49185] A function of VGAM1406 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Accession NM_001356), a gene which interacts with hepatitis c virus core protein resulting a change in intracellular location. Accordingly, utilities of VGAM1406 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with DDX3. The function of DDX3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM232. ARG99 (Accession NM_031920) is another VGAM1406 host target gene. ARG99 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARG99, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARG99 BINDING SITE, designated SEQ ID:25669, to the nucleotide sequence of VGAM1406 RNA, herein designated VGAM RNA, also designated SEQ ID:4117.

[49186] Another function of VGAM1406 is therefore inhibition of ARG99 (Accession NM_031920). Accordingly, utilities of VGAM1406 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARG99. FLJ23462 (Accession NM_024843) is another VGAM1406 host target gene. FLJ23462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23462 BINDING SITE, designated SEQ ID:24260, to the nucleotide sequence of VGAM1406 RNA, herein designated VGAM RNA, also designated SEQ ID:4117.

[49187] Another function of VGAM1406 is therefore inhibition of FLJ23462 (Accession NM_024843). Accordingly, utilities of VGAM1406 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23462. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM1406 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7857, to the nucleotide sequence of VGAM1406 RNA, herein designated VGAM RNA, also designated SEQ ID:4117.

[49188] Another function of VGAM1406 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM1406

include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1407 (VGAM1407) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49189] VGAM1407 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1407 was detected is described hereinabove with reference to Figs. 1–8.

[49190] VGAM1407 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acute Bee Paralysis Virus. VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49191] VGAM1407 gene encodes a VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1407 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1407 precursor RNA is desig-

nated SEQ ID:1393, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1393 is located at position 7313 relative to the genome of Acute Bee Paralysis Virus.

- [49192] VGAM1407 precursor RNA folds onto itself, forming VGAM1407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49193] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1407 folded precursor RNA into VGAM1407 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM1407 RNA is designated SEQ ID:4118, and is provided hereinbelow with reference to the sequence

listing part.

[49194] VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1407 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49195] VGAM1407 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1407 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1407 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49196] The complementary binding of VGAM1407 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1407 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1407 host target RNA into VGAM1407 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49197] It is appreciated that VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1407 host target genes. The mRNA of each one of this plurality of VGAM1407 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1407 RNA, herein designated VGAM

RNA, and which when bound by VGAM1407 RNA causes inhibition of translation of respective one or more VGAM1407 host target proteins.

[49198] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1407 gene, herein designated VGAM GENE, on one or more VGAM1407 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49199] It is yet further appreciated that a function of VGAM1407 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1407 include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1407 correlate with, and may be deduced from, the identity of the host target genes which VGAM1407 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49200] Nucleotide sequences of the VGAM1407 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1407 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1407 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1407 are further described hereinbelow with reference to Table 1.

[49201] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1407 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1407 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49202] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1407 gene, herein designated VGAM is

inhibition of expression of VGAM1407 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1407 correlate with, and may be deduced from, the identity of the target genes which VGAM1407 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49203] 24-dehydrocholesterol Reductase (DHCR24, Accession NM_014762) is a VGAM1407 host target gene. DHCR24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DHCR24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHCR24 BINDING SITE, designated SEQ ID:16521, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49204] A function of VGAM1407 is therefore inhibition of 24-dehydrocholesterol Reductase (DHCR24, Accession NM_014762), a gene which catalyzes the reduction of sterol intermediates. Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHCR24. The func-

tion of DHCR24 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM235. General Transcription Factor IIH, Polypeptide 1, 62kDa (GTF2H1, Accession NM_005316) is another VGAM1407 host target gene. GTF2H1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTF2H1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF2H1 BINDING SITE, designated SEQ ID:11792, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49205] Another function of VGAM1407 is therefore inhibition of General Transcription Factor IIH, Polypeptide 1, 62kDa (GTF2H1, Accession NM_005316), a gene which is subunit of RNA polymerase II transcription initiation factor IIH; involved in transcription and DNA repair mechanisms. Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF2H1. The function of GTF2H1 has been established by previous studies. Initiation of tran-

scription by RNA polymerase II is a complex process requiring, in addition to the polymerase itself, 7 auxiliary factors. Entry of the polymerase into the transcription cycle is mediated by transcription factor TFIIF (see OMIM Ref. No. 189968) and requires a DNA-protein complex composed of the TATA-binding protein subunit of TFIID (OMIM Ref. No. 313650) in association with the TATA motif and TFIIB (OMIM Ref. No. 189963), the so-called DB complex. The largest subunit of mammalian RNA polymerase II (OMIM Ref. No. 180660) contains a heptapeptide repeat, YSPTSPS in the single-letter amino acid code, occurring 52 times at its C terminus. Because the heptapeptide contains serine, threonine, and tyrosine, it is prone to phosphorylation. As a result, RNA polymerase II occurs in 2 forms in vivo: a highly phosphorylated II(O) form and a nonphosphorylated II(A) form. The nonphosphorylated form of RNA polymerase II is recruited by TFIIF to the DB complex. This complex is then recognized by TFII E (OMIM Ref. No. 189962), TFII H, and TFII J, which enter the transcription cycle in that order, to generate a transcription-competent complex. Phosphorylation of the C-terminal domain of the largest subunit of RNA polymerase II is believed to control the transition from transcription initiation

to elongation. The general transcription factor TFIID contains a kinase activity capable of phosphorylating this domain (Lu et al., 1992). Factors that promote the association of RNA polymerase II with the preinitiation complex stimulate this activity. TFIIE, which is required for the stable association of TFIID with the preinitiation complex, affects the processivity of TFIID kinase. TFIID is a multisubunit factor consisting of at least 5 polypeptides of 92 (OMIM Ref. No. 133510), 62, 43 (OMIM Ref. No. 601748), 40, and 35 (OMIM Ref. No. 601750) kD (Flores et al., 1992). A 52-kD subunit (OMIM Ref. No. 601760) has also been identified as a component of the TFIID 'core,' along with p89, p62, p44, and p34 (Marinoni et al., 1997). Lu et al. (1992) expressed the belief that TFIID is the human counterpart of the yeast general transcription factor b. See also 133530 and Habraken et al. (1996). High levels of gene transcription by RNA polymerase II depend on high rates of transcription initiation and reinitiation. Initiation requires recruitment of the complete transcription machinery to a promoter, a process facilitated by activators and chromatin remodeling factors. Reinitiation is thought to occur through a different pathway. After initiation, a subset of the transcription machinery remains at the pro-

moter, forming a platform for assembly of a second transcription complex. Yudkovsky et al. (2000) described the isolation of a reinitiation intermediate in yeast that includes transcription factors TFIID, TFIIA (see OMIM Ref. No. 600520), TFIIH, TFIIIE, and Mediator. This intermediate can act as a scaffold for formation of a functional reinitiation complex. Formation of this scaffold is dependent on ATP and TFIIH. In yeast, the scaffold is stabilized in the presence of the activator Gal4-VP16, but not Gal4-AH, suggesting a new role for some activators and Mediator in promoting high levels of transcription.

[49206] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49207] Lu, H.; Zawel, L.; Fisher, L.; Egly, J.-M.; Reinberg, D. : Human general transcription factor IIH phosphorylates the C-terminal domain of RNA polymerase II. *Nature* 358: 641-645, 1992. ; and

[49208] Yudkovsky, N.; Ranish, J. A.; Hahn, S. : A transcription reinitiation intermediate that is stabilized by activator. *Nature* 408: 225-229, 2000.

[49209] Further studies establishing the function and utilities of GTF2H1 are found in John Hopkins OMIM database record

ID 189972, and in cited publications numbered 4706–769, 11357–77 and 1907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966) is another VGAM1407 host target gene. C1orf24 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1orf24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf24 BINDING SITE, designated SEQ ID:27527, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49210] Another function of VGAM1407 is therefore inhibition of Chromosome 1 Open Reading Frame 24 (C1orf24, Accession NM_052966). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf24. FLJ10891 (Accession NM_018260) is another VGAM1407 host target gene. FLJ10891 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10891, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10891 BINDING SITE, designated SEQ ID:20226, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49211] Another function of VGAM1407 is therefore inhibition of FLJ10891 (Accession NM_018260). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10891. FLJ12666 (Accession NM_024595) is another VGAM1407 host target gene. FLJ12666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12666 BINDING SITE, designated SEQ ID:23831, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49212] Another function of VGAM1407 is therefore inhibition of FLJ12666 (Accession NM_024595). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ12666. FLJ14011 (Accession NM_022103) is another VGAM1407 host target gene. FLJ14011 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14011 BINDING SITE, designated SEQ ID:22649, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49213] Another function of VGAM1407 is therefore inhibition of FLJ14011 (Accession NM_022103). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14011. Histidyl-tRNA Synthetase 2 (HARS2, Accession NM_080820) is another VGAM1407 host target gene. HARS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HARS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HARS2 BINDING SITE, designated SEQ

ID:28077, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49214] Another function of VGAM1407 is therefore inhibition of Histidyl-tRNA Synthetase 2 (HARS2, Accession NM_080820). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HARS2. KIAA0426 (Accession NM_014724) is another VGAM1407 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16304, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49215] Another function of VGAM1407 is therefore inhibition of KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA1871 (Accession XM_028409) is another

VGAM1407 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30700, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49216] Another function of VGAM1407 is therefore inhibition of KIAA1871 (Accession XM_028409). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. LOC147660 (Accession XM_085825) is another VGAM1407 host target gene. LOC147660 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147660, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147660 BINDING SITE, designated SEQ ID:38349, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49217] Another function of VGAM1407 is therefore inhibition of LOC147660 (Accession XM_085825). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147660. LOC157657 (Accession XM_088352) is another VGAM1407 host target gene. LOC157657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157657 BINDING SITE, designated SEQ ID:39627, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49218] Another function of VGAM1407 is therefore inhibition of LOC157657 (Accession XM_088352). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157657. LOC90333 (Accession XM_030958) is another VGAM1407 host target gene. LOC90333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90333, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90333 BINDING SITE, designated SEQ ID:31217, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49219] Another function of VGAM1407 is therefore inhibition of LOC90333 (Accession XM_030958). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90333. LOC91664 (Accession XM_039908) is another VGAM1407 host target gene. LOC91664 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91664, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91664 BINDING SITE, designated SEQ ID:33212, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49220] Another function of VGAM1407 is therefore inhibition of LOC91664 (Accession XM_039908). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC91664. LOC92283 (Accession XM_044049) is another VGAM1407 host target gene. LOC92283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92283 BINDING SITE, designated SEQ ID:34090, to the nucleotide sequence of VGAM1407 RNA, herein designated VGAM RNA, also designated SEQ ID:4118.

[49221] Another function of VGAM1407 is therefore inhibition of LOC92283 (Accession XM_044049). Accordingly, utilities of VGAM1407 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92283. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1408 (VGAM1408) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49222] VGAM1408 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1408 was detected is described hereinabove with reference to Figs. 1–8.

[49223] VGAM1408 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acute Bee Paralysis Virus. VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49224] VGAM1408 gene encodes a VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1408 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1408 precursor RNA is designated SEQ ID:1394, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1394 is located at position 6189 relative to the genome of Acute Bee Paralysis Virus.

[49225] VGAM1408 precursor RNA folds onto itself, forming VGAM1408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49226] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1408 folded precursor RNA into VGAM1408 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM1408 RNA is designated SEQ ID:4119, and is provided hereinbelow with reference to the sequence listing part.

[49227] VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1408 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49228] VGAM1408 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1408 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1408 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49229] The complementary binding of VGAM1408 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1408 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1408 host target RNA into VGAM1408 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49230] It is appreciated that VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1408 host target genes. The mRNA of each one of this plurality of VGAM1408 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1408 RNA, herein designated VGAM RNA, and which when bound by VGAM1408 RNA causes inhibition of translation of respective one or more VGAM1408 host target proteins.

[49231] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1408 gene, herein designated VGAM GENE, on one or more VGAM1408 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49232] It is yet further appreciated that a function of VGAM1408 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1408 include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1408 correlate with, and may be deduced from, the identity of the host target genes which VGAM1408 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49233] Nucleotide sequences of the VGAM1408 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1408 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1408 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1408 are further described hereinbelow with reference to Table 1.

[49234] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1408 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1408 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49235] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1408 gene, herein designated VGAM is inhibition of expression of VGAM1408 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1408 correlate with, and may be deduced from, the identity of the target genes which VGAM1408 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49236] Ectonucleotide Pyrophosphatase/phosphodiesterase 3 (ENPP3, Accession NM_005021) is a VGAM1408 host target gene. ENPP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by ENPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENPP3 BINDING SITE, designated SEQ ID:11461, to the nucleotide sequence of VGAM1408 RNA, herein designated VGAM RNA, also designated SEQ ID:4119.

[49237] A function of VGAM1408 is therefore inhibition of Ectonucleotide Pyrophosphatase/phosphodiesterase 3 (ENPP3, Accession NM_005021). Accordingly, utilities of VGAM1408 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENPP3. Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM_003038) is another VGAM1408 host target gene. SLC1A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A4 BINDING SITE, designated SEQ ID:8994, to the nucleotide sequence of VGAM1408 RNA, herein designated VGAM RNA, also designated SEQ ID:4119.

[49238] Another function of VGAM1408 is therefore inhibition of Solute Carrier Family 1 (glutamate/neutral amino acid transporter), Member 4 (SLC1A4, Accession NM_003038), a gene which transports alanine, serine, cysteine, and threonine. exhibits sodium dependence. Accordingly, utilities of VGAM1408 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A4. The function of SLC1A4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM859. LOC120856 (Accession XM_058509) is another VGAM1408 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36636, to the nucleotide sequence of VGAM1408 RNA, herein designated VGAM RNA, also designated SEQ ID:4119.

[49239] Another function of VGAM1408 is therefore inhibition of LOC120856 (Accession XM_058509). Accordingly, utilities

of VGAM1408 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC158263 (Accession XM_088530) is another VGAM1408 host target gene. LOC158263 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158263 BINDING SITE, designated SEQ ID:39798, to the nucleotide sequence of VGAM1408 RNA, herein designated VGAM RNA, also designated SEQ ID:4119.

[49240] Another function of VGAM1408 is therefore inhibition of LOC158263 (Accession XM_088530). Accordingly, utilities of VGAM1408 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158263. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1409 (VGAM1409) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49241] VGAM1409 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1409 was detected is described hereinabove with reference to Figs. 1–8.

[49242] VGAM1409 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acute Bee Paralysis Virus. VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49243] VGAM1409 gene encodes a VGAM1409 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1409 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1409 precursor RNA is designated SEQ ID:1395, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1395 is located at position 9338 relative to the genome of Acute Bee Paralysis Virus.

[49244] VGAM1409 precursor RNA folds onto itself, forming VGAM1409 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49245] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1409 folded precursor RNA into VGAM1409 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM1409 RNA is designated SEQ ID:4120, and is provided hereinbelow with reference to the sequence listing part.

[49246] VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1409 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[49247] VGAM1409 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1409 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1409 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49248] The complementary binding of VGAM1409 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1409 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1409 host target RNA into VGAM1409 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49249] It is appreciated that VGAM1409 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1409 host target genes. The mRNA of each one of this plurality of VGAM1409 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1409 RNA, herein designated VGAM RNA, and which when bound by VGAM1409 RNA causes inhibition of translation of respective one or more VGAM1409 host target proteins.

[49250] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1409 gene, herein designated VGAM GENE, on one or more VGAM1409 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49251] It is yet further appreciated that a function of VGAM1409 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1409 correlate with, and may be deduced from, the identity of the host target genes which VGAM1409 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49252] Nucleotide sequences of the VGAM1409 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1409 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1409 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1409 are further
described hereinbelow with reference to Table 1.

[49253] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1409 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1409 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[49254] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1409 gene, herein designated VGAM is
inhibition of expression of VGAM1409 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1409 correlate with, and may be deduced
from, the identity of the target genes which VGAM1409
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[49255] FLJ10718 (Accession NM_018192) is a VGAM1409 host
target gene. FLJ10718 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by FLJ10718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10718 BINDING SITE, designated SEQ ID:20049, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49256] A function of VGAM1409 is therefore inhibition of FLJ10718 (Accession NM_018192). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10718. FLJ14281 (Accession NM_024920) is another VGAM1409 host target gene. FLJ14281 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14281 BINDING SITE, designated SEQ ID:24452, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49257] Another function of VGAM1409 is therefore inhibition of

FLJ14281 (Accession NM_024920). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14281. FLJ20139 (Accession NM_017685) is another VGAM1409 host target gene. FLJ20139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20139 BINDING SITE, designated SEQ ID:19236, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49258] Another function of VGAM1409 is therefore inhibition of FLJ20139 (Accession NM_017685). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20139. FLJ31101 (Accession NM_017964) is another VGAM1409 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19685, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49259] Another function of VGAM1409 is therefore inhibition of FLJ31101 (Accession NM_017964). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31101. KIAA0964 (Accession NM_014902) is another VGAM1409 host target gene. KIAA0964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0964 BINDING SITE, designated SEQ ID:17087, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49260] Another function of VGAM1409 is therefore inhibition of KIAA0964 (Accession NM_014902). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0964. Syntaxin 12 (STX12, Accession XM_039018) is

another VGAM1409 host target gene. STX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STX12 BINDING SITE, designated SEQ ID:32982, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49261] Another function of VGAM1409 is therefore inhibition of Syntaxin 12 (STX12, Accession XM_039018). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STX12. LOC139231 (Accession XM_060020) is another VGAM1409 host target gene. LOC139231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139231 BINDING SITE, designated SEQ ID:37142, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49262] Another function of VGAM1409 is therefore inhibition of LOC139231 (Accession XM_060020). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139231. LOC146669 (Accession XM_085534) is another VGAM1409 host target gene. LOC146669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146669 BINDING SITE, designated SEQ ID:38226, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49263] Another function of VGAM1409 is therefore inhibition of LOC146669 (Accession XM_085534). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146669. LOC149650 (Accession XM_086623) is another VGAM1409 host target gene. LOC149650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149650, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149650 BINDING SITE, designated SEQ ID:38794, to the nucleotide sequence of VGAM1409 RNA, herein designated VGAM RNA, also designated SEQ ID:4120.

[49264] Another function of VGAM1409 is therefore inhibition of LOC149650 (Accession XM_086623). Accordingly, utilities of VGAM1409 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149650. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1410 (VGAM1410) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49265] VGAM1410 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1410 was detected is described hereinabove with reference to Figs. 1-8.

[49266] VGAM1410 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acute Bee Paralysis Virus. VGAM1410 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49267] VGAM1410 gene encodes a VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1410 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1410 precursor RNA is designated SEQ ID:1396, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1396 is located at position 8237 relative to the genome of Acute Bee Paralysis Virus.

[49268] VGAM1410 precursor RNA folds onto itself, forming VGAM1410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49269] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1410 folded precursor RNA into VGAM1410

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1410 RNA is designated SEQ ID:4121, and is provided hereinbelow with reference to the sequence listing part.

[49270] VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1410 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49271] VGAM1410 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1410 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1410 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49272] The complementary binding of VGAM1410 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1410 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1410 host target RNA into VGAM1410 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[49273] It is appreciated that VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1410 host target genes. The mRNA of each one of this plurality of VGAM1410 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1410 RNA, herein designated VGAM RNA, and which when bound by VGAM1410 RNA causes inhibition of translation of respective one or more VGAM1410 host target proteins.

[49274] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1410 gene, herein designated VGAM GENE, on one or more VGAM1410 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49275] It is yet further appreciated that a function of VGAM1410 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1410 correlate with, and may be deduced from, the identity of the host target genes which VGAM1410 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49276] Nucleotide sequences of the VGAM1410 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1410 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1410 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1410 are further described hereinbelow with reference to Table 1.

[49277] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1410 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1410 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49278] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1410 gene, herein designated VGAM is inhibition of expression of VGAM1410 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1410 correlate with, and may be deduced from, the identity of the target genes which VGAM1410 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49279] B29 (Accession NM_031939) is a VGAM1410 host target gene. B29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B29 BINDING SITE, designated SEQ ID:25685, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49280] A function of VGAM1410 is therefore inhibition of B29 (Accession NM_031939). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B29. Fanconi Anemia, Complementation Group C (FANCC, Accession XM_047190) is another VGAM1410 host target gene. FANCC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCC BINDING SITE, designated SEQ ID:34907, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49281] Another function of VGAM1410 is therefore inhibition of Fanconi Anemia, Complementation Group C (FANCC, Accession XM_047190). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCC. Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM_009220) is another VGAM1410 host target gene. GNA15 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by GNA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNA15 BINDING SITE, designated SEQ ID:30104, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49282] Another function of VGAM1410 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha 15 (Gq class) (GNA15, Accession XM_009220). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNA15. Heparan Sulfate (glucosamine) 3-O-sulfotransferase 4 (HS3ST4, Accession XM_056254) is another VGAM1410 host target gene. HS3ST4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS3ST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS3ST4 BINDING SITE, designated SEQ ID:36371, to the nucleotide sequence of VGAM1410 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4121.

[49283] Another function of VGAM1410 is therefore inhibition of Heparan Sulfate (glucosamine) 3-O-sulfotransferase 4 (HS3ST4, Accession XM_056254). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS3ST4. Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM_002372) is another VGAM1410 host target gene. MAN2A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN2A1 BINDING SITE, designated SEQ ID:8180, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49284] Another function of VGAM1410 is therefore inhibition of Mannosidase, Alpha, Class 2A, Member 1 (MAN2A1, Accession NM_002372), a gene which catalyzes the final hydrolytic step in the asparagine-linked oligosaccharide (N-glycan) maturation pathway. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MAN2A1. The function of MAN2A1 has been established by previous studies. Alpha-mannosidase II catalyzes the first committed step in the biosynthesis of complex N-glycans. Genetic deficiency of this enzyme should abolish complex N-glycan production as reportedly does inhibition of the enzyme by swainsonine. Chui et al. (1997) found that mice in whom the alpha-mannosidase II gene had been disrupted developed a dyserythropoietic anemia concurrent with loss of erythrocyte complex N-glycans. Unexpectedly, nonerythroid cell types continued to produce complex N-glycans by an alternate pathway comprising a distinct alpha-mannosidase. These studies revealed cell type-specific variations in N-linked oligosaccharide biosynthesis and an essential role for alpha-mannosidase II in the formation of erythroid complex N-glycans. Alpha-mannosidase II deficiency elicited a phenotype in mice that corresponds to human congenital dyserythropoietic anemia type II. Although a genetic defect of MAN2A1 was thought to cause congenital dyserythropoietic anemia type II, or HEMPAS (OMIM Ref. No. 224100), Gasparini et al. (1997) excluded it as a candidate gene by demonstrating linkage of the disorder to markers

on chromosome 20. Protein glycosylation in the Golgi apparatus produces structural variation at the cell surface and contributes to immune self-recognition. Altered protein glycosylation and antibodies that recognize endogenous glycans have been associated with various autoimmune syndromes, with the possibility that such abnormalities may reflect genetic defects in glycan formation. Studying mice with a null allele for alpha-mannosidase II, Chui et al. (2001) showed that mutation in this gene, which regulates the hybrid to complex branching pattern of extracellular asparagine (N)-linked oligosaccharide chains (N-glycans), results in a systemic autoimmune disease similar to human systemic lupus erythematosus (OMIM Ref. No. 152700). The findings demonstrated a genetic cause of autoimmune disease provoked by a defect in the pathway of protein N-glycosylation.

[49285] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49286] Chui, D.; Oh-Eda, M.; Liao, Y.-F.; Panneerselvam, K.; Lai, A.; Marek, K. W.; Freeze, H. H.; Moremen, K. W.; Fukuda, M. N.; Marth, J. D. : Alpha-mannosidase-II deficiency results in dyserythropoiesis and unveils an alternate path-

way in oligosaccharide biosynthesis. Cell 90: 157–167, 1997. ; and

[49287] Chui, D.; Sellakumar, G.; Green, R. S.; Sutton–Smith, M.; McQuistan, T.; Marek, K. W.; Morris, H. R.; Dell, A.; Marth, J. D. : Genetic remodeling of protein glycosylation in vivo induces.

[49288] Further studies establishing the function and utilities of MAN2A1 are found in John Hopkins OMIM database record ID 154582, and in cited publications numbered 11526–11530 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. N–acetylgalactosaminidase, Alpha– (NAGA, Accession NM_000262) is another VGAM1410 host target gene. NAGA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NAGA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAGA BINDING SITE, designated SEQ ID:5800, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49289] Another function of VGAM1410 is therefore inhibition of N–acetylgalactosaminidase, Alpha– (NAGA, Accession

NM_000262). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAGA. Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Alpha Polypeptide I (P4HA1, Accession NM_000917) is another VGAM1410 host target gene. P4HA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P4HA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P4HA1 BINDING SITE, designated SEQ ID:6626, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49290] Another function of VGAM1410 is therefore inhibition of Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Alpha Polypeptide I (P4HA1, Accession NM_000917), a gene which catalyzes the formation of 4-hydroxyproline in collagen. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P4HA1. The function of P4HA1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM260. Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350) is another VGAM1410 host target gene. PDGFRB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRB BINDING SITE, designated SEQ ID:32814, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49291] Another function of VGAM1410 is therefore inhibition of Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350), a gene which Platelet-derived growth factor receptor beta chain; tyrosine kinase receptor. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRB. The function of PDGFRB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Prostaglandin-endoperoxide Synthase 1

(prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM_080591) is another VGAM1410 host target gene. PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTGS1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGS1 BINDING SITE1 and PTGS1 BINDING SITE2, designated SEQ ID:27900 and SEQ ID:6679 respectively, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49292] Another function of VGAM1410 is therefore inhibition of Prostaglandin-endoperoxide Synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1, Accession NM_080591), a gene which may play an important role in regulating or promoting cell proliferation in some normal and neoplastically transformed cells. Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS1. The function of PTGS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM1224. Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270) is another VGAM1410 host target gene. C20orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf20 BINDING SITE, designated SEQ ID:20248, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49293] Another function of VGAM1410 is therefore inhibition of Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf20. Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289) is another VGAM1410 host target gene. CLIC2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIC2 BIND-

ING SITE, designated SEQ ID:6968, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49294] Another function of VGAM1410 is therefore inhibition of Chloride Intracellular Channel 2 (CLIC2, Accession NM_001289). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIC2. CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) Phosphatase, Subunit 1 (CTDP1, Accession NM_004715) is another VGAM1410 host target gene. CTDP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTDP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTDP1 BINDING SITE, designated SEQ ID:11073, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49295] Another function of VGAM1410 is therefore inhibition of CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) Phosphatase, Subunit 1 (CTDP1, Accession

NM_004715). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTDP1. Dynactin 4 (p62) (DCTN4, Accession XM_041993) is another VGAM1410 host target gene. DCTN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCTN4 BINDING SITE, designated SEQ ID:33665, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49296] Another function of VGAM1410 is therefore inhibition of Dynactin 4 (p62) (DCTN4, Accession XM_041993). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCTN4. DKFZP586C1619 (Accession XM_030350) is another VGAM1410 host target gene. DKFZP586C1619 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586C1619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586C1619 BINDING SITE, designated SEQ ID:31017, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49297] Another function of VGAM1410 is therefore inhibition of DKFZP586C1619 (Accession XM_030350). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586C1619. FLJ20574 (Accession NM_017886) is another VGAM1410 host target gene. FLJ20574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20574 BINDING SITE, designated SEQ ID:19556, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49298] Another function of VGAM1410 is therefore inhibition of FLJ20574 (Accession NM_017886). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ20574. KIAA0121 (Accession XM_052386) is another VGAM1410 host target gene. KIAA0121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0121 BINDING SITE, designated SEQ ID:35972, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49299] Another function of VGAM1410 is therefore inhibition of KIAA0121 (Accession XM_052386). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. KIAA0417 (Accession XM_048898) is another VGAM1410 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0417 BINDING SITE, designated SEQ ID:35291, to the nucleotide sequence of VGAM1410 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4121.

[49300] Another function of VGAM1410 is therefore inhibition of KIAA0417 (Accession XM_048898). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA1538 (Accession XM_049474) is another VGAM1410 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35422, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49301] Another function of VGAM1410 is therefore inhibition of KIAA1538 (Accession XM_049474). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. KIAA1881 (Accession XM_170901) is another VGAM1410 host target gene. KIAA1881 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1881, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1881 BINDING SITE, designated SEQ ID:45655, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49302] Another function of VGAM1410 is therefore inhibition of KIAA1881 (Accession XM_170901). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1881. Myozenin 2 (MYOZ2, Accession NM_016599) is another VGAM1410 host target gene. MYOZ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYOZ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYOZ2 BINDING SITE, designated SEQ ID:18693, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49303] Another function of VGAM1410 is therefore inhibition of Myozenin 2 (MYOZ2, Accession NM_016599). Accordingly, utilities of VGAM1410 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with MYOZ2. NDST4 (Accession NM_022569) is another VGAM1410 host target gene. NDST4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NDST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDST4 BINDING SITE, designated SEQ ID:22892, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49304] Another function of VGAM1410 is therefore inhibition of NDST4 (Accession NM_022569). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDST4. Neuronal PAS Domain Protein 3 (NPAS3, Accession NM_022123) is another VGAM1410 host target gene. NPAS3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NPAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPAS3 BINDING SITE, designated SEQ

ID:22666, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49305] Another function of VGAM1410 is therefore inhibition of Neuronal PAS Domain Protein 3 (NPAS3, Accession NM_022123). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPAS3. SSB-4 (Accession NM_080862) is another VGAM1410 host target gene. SSB-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSB-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSB-4 BINDING SITE, designated SEQ ID:28104, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49306] Another function of VGAM1410 is therefore inhibition of SSB-4 (Accession NM_080862). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSB-4. SYNE-1 (Accession NM_015293) is another VGAM1410 host target gene. SYNE-1 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by SYNE-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNE-1 BINDING SITE, designated SEQ ID:17615, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49307] Another function of VGAM1410 is therefore inhibition of SYNE-1 (Accession NM_015293). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNE-1. Wingless-type MMTV Integration Site Family, Member 10A (WNT10A, Accession NM_025216) is another VGAM1410 host target gene. WNT10A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WNT10A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT10A BINDING SITE, designated SEQ ID:24896, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49308] Another function of VGAM1410 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 10A (WNT10A, Accession NM_025216). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT10A. LOC148753 (Accession XM_097515) is another VGAM1410 host target gene. LOC148753 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148753 BINDING SITE, designated SEQ ID:40900, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49309] Another function of VGAM1410 is therefore inhibition of LOC148753 (Accession XM_097515). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148753. LOC152559 (Accession XM_087487) is another VGAM1410 host target gene. LOC152559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152559, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152559 BINDING SITE, designated SEQ ID:39283, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49310] Another function of VGAM1410 is therefore inhibition of LOC152559 (Accession XM_087487). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152559. LOC155032 (Accession XM_098647) is another VGAM1410 host target gene. LOC155032 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155032 BINDING SITE, designated SEQ ID:41748, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49311] Another function of VGAM1410 is therefore inhibition of LOC155032 (Accession XM_098647). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC155032. LOC90155 (Accession XM_029487) is another VGAM1410 host target gene. LOC90155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90155 BINDING SITE, designated SEQ ID:30900, to the nucleotide sequence of VGAM1410 RNA, herein designated VGAM RNA, also designated SEQ ID:4121.

[49312] Another function of VGAM1410 is therefore inhibition of LOC90155 (Accession XM_029487). Accordingly, utilities of VGAM1410 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90155. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1411 (VGAM1411) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49313] VGAM1411 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1411 was detected is described hereinabove with reference to Figs. 1–8.

[49314] VGAM1411 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Acute Bee Paralysis Virus. VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49315] VGAM1411 gene encodes a VGAM1411 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1411 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1411 precursor RNA is designated SEQ ID:1397, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1397 is located at position 3090 relative to the genome of Acute Bee Paralysis Virus.

[49316] VGAM1411 precursor RNA folds onto itself, forming VGAM1411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49317] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1411 folded precursor RNA into VGAM1411 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1411 RNA is designated SEQ ID:4122, and is provided hereinbelow with reference to the sequence listing part.

[49318] VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1411 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49319] VGAM1411 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1411 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1411 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49320] The complementary binding of VGAM1411 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1411 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1411 host target RNA into VGAM1411 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49321] It is appreciated that VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1411 host target genes. The mRNA of each one of this plurality of VGAM1411 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1411 RNA, herein designated VGAM RNA, and which when bound by VGAM1411 RNA causes inhibition of translation of respective one or more VGAM1411 host target proteins.

[49322] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1411 gene, herein designated VGAM GENE, on one or more VGAM1411 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49323] It is yet further appreciated that a function of VGAM1411 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1411 correlate with, and may be deduced from, the identity of the host target genes which VGAM1411 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49324] Nucleotide sequences of the VGAM1411 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1411 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1411 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1411 are further described hereinbelow with reference to Table 1.

[49325] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1411 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1411 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49326] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1411 gene, herein designated VGAM is inhibition of expression of VGAM1411 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1411 correlate with, and may be deduced from, the identity of the target genes which VGAM1411 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49327] Poliovirus Receptor (PVR, Accession NM_006505) is a VGAM1411 host target gene. PVR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by PVR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PVR BINDING SITE, designated SEQ ID:13253, to the nucleotide sequence of VGAM1411 RNA, herein designated VGAM RNA, also designated SEQ ID:4122.

[49328] A function of VGAM1411 is therefore inhibition of Poliovirus Receptor (PVR, Accession NM_006505), a gene which is a poliovirus receptor. Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PVR. The function of PVR has been established by previous studies. Primates are susceptible to poliomyelitis infection, but rodents are not; furthermore, human cells but not rodent cells are killed by poliovirus in vitro. Susceptibility to poliovirus is a function of the presence or absence of a cellular receptor to which the virus binds as the first step in poliovirus replication. Mendelsohn et al. (1986) succeeded in transforming a human poliovirus receptor gene into mouse L cells which are ordinarily resistant to poliovirus infection because they do not bear a poliovirus receptor. Monoclonal antibody directed against

the HeLa cell poliovirus receptor site was used in rosette assays to identify poliovirus-sensitive transformants. In a study of human-mouse hybrids, Miller et al. (1974) showed that chromosome 19 is correlated with susceptibility to poliovirus. Siddique et al. (1985) regionalized the PVS gene to 19q13-qter. By the study of rodent/human hybrid cell lines carrying 4 different regions of human chromosome 19, Siddique et al. (1988) demonstrated that the typical cytopathic effects of poliovirus infection were observed only when the region 19q12-q13.2 was contained as the smallest region of overlap. The same region contains the gene for myotonic dystrophy (OMIM Ref. No. 160900). The PVS gene is also of interest in connection with inherited motor neuron diseases because it encodes a cell-surface receptor expressed on motor neurons. Shepley et al. (1988) prepared a monoclonal antibody that identified a 100-kD membrane protein in HeLa cells and in human spinal cord involved in poliovirus attachment. They showed that the antigen identified by the monoclonal antibody was associated with the presence of human chromosome 19 in human-mouse hybrid cell lines. The monoclonal antibodies stained neurons in the reticular formation and clusters of brain stem neurons, consis-

tent with the known pattern of damage caused by poliovirus infection in the brain stem. Furthermore, it reacted with human peripheral mononuclear cells, consistent with the known replication of poliovirus in Peyer patches and tonsils. Schonk et al. (1990) assigned the PVS gene to 19q13.2 by hybridization studies using a panel of somatic cell hybrids with subchromosomal segments of 19q. By fluorescence in situ hybridization, Trask et al. (1993) assigned the PVS gene to 19q13.2–q13.3. Seldin et al. (1991) mapped the homologous gene in the mouse to chromosome 9.

[49329] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49330] Mendelsohn, C.; Johnson, B.; Lionetti, K. A.; Nobis, P.; Wimmer, E.; Racaniello, V. R. : Transformation of a human poliovirus receptor gene into mouse cells. Proc. Nat. Acad. Sci. 83: 7845–7849, 1986. ; and

[49331] Seldin, M. F.; Saunders, A. M.; Rochelle, J. M.; Howard, T. A. : A proximal mouse chromosome 9 linkage map that further defines linkage groups homologous with segments of human chromosom.

[49332] Further studies establishing the function and utilities of

PVR are found in John Hopkins OMIM database record ID 173850, and in cited publications numbered 2745–2751, 3792, 4813–177 and 4710 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0635 (Accession NM_014645) is another VGAM1411 host target gene. KIAA0635 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0635 BINDING SITE, designated SEQ ID:16055, to the nucleotide sequence of VGAM1411 RNA, herein designated VGAM RNA, also designated SEQ ID:4122.

[49333] Another function of VGAM1411 is therefore inhibition of KIAA0635 (Accession NM_014645). Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0635. KIAA0894 (Accession NM_014896) is another VGAM1411 host target gene. KIAA0894 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0894, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0894 BINDING SITE, designated SEQ ID:17055, to the nucleotide sequence of VGAM1411 RNA, herein designated VGAM RNA, also designated SEQ ID:4122.

[49334] Another function of VGAM1411 is therefore inhibition of KIAA0894 (Accession NM_014896). Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0894. LOC54505 (Accession XM_042110) is another VGAM1411 host target gene. LOC54505 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC54505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54505 BINDING SITE, designated SEQ ID:33694, to the nucleotide sequence of VGAM1411 RNA, herein designated VGAM RNA, also designated SEQ ID:4122.

[49335] Another function of VGAM1411 is therefore inhibition of LOC54505 (Accession XM_042110). Accordingly, utilities of VGAM1411 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC54505. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1412 (VGAM1412) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49336] VGAM1412 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1412 was detected is described hereinabove with reference to Figs. 1–8.

[49337] VGAM1412 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Yellow Mosaic Virus. VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49338] VGAM1412 gene encodes a VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1412 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1412 precursor RNA is designated SEQ ID:1398, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1398 is located at position 555 relative to the genome of Bean Yellow Mosaic Virus.

[49339] VGAM1412 precursor RNA folds onto itself, forming VGAM1412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49340] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1412 folded precursor RNA into VGAM1412 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1412 RNA is designated SEQ ID:4123, and is provided hereinbelow with reference to the sequence listing part.

[49341] VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1412 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49342] VGAM1412 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1412 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1412 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49343] The complementary binding of VGAM1412 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1412 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1412 host target RNA into VGAM1412 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49344] It is appreciated that VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1412 host target genes. The mRNA of each one of this plurality of VGAM1412 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1412 RNA, herein designated VGAM RNA, and which when bound by VGAM1412 RNA causes

inhibition of translation of respective one or more VGAM1412 host target proteins.

[49345] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1412 gene, herein designated VGAM GENE, on one or more VGAM1412 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49346] It is yet further appreciated that a function of VGAM1412 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1412 include diagnosis, prevention and

treatment of viral infection by Bean Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1412 correlate with, and may be deduced from, the identity of the host target genes which VGAM1412 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49347] Nucleotide sequences of the VGAM1412 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1412 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1412 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1412 are further described hereinbelow with reference to Table 1.

[49348] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1412 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1412 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49349] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1412 gene, herein designated VGAM is inhibition of expression of VGAM1412 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1412 correlate with, and may be deduced from, the identity of the target genes which VGAM1412 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49350] Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is a VGAM1412 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12880, to the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, also designated SEQ ID:4123.

[49351] A function of VGAM1412 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117. Serine/threonine Kinase 38 (STK38, Accession NM_007271) is another VGAM1412 host target gene. STK38 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38 BINDING SITE, designated SEQ ID:14134, to the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, also designated SEQ ID:4123.

[49352] Another function of VGAM1412 is therefore inhibition of Serine/threonine Kinase 38 (STK38, Accession NM_007271). Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK38. DKFZp434K2435 (Accession NM_032256) is another VGAM1412 host target gene. DKFZp434K2435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434K2435, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434K2435 BINDING SITE, designated SEQ ID:26001, to the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, also designated SEQ ID:4123.

[49353] Another function of VGAM1412 is therefore inhibition of DKFZp434K2435 (Accession NM_032256). Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434K2435. FLJ20051 (Accession NM_019087) is another VGAM1412 host target gene. FLJ20051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20051 BINDING SITE, designated SEQ ID:21162, to the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, also designated SEQ ID:4123.

[49354] Another function of VGAM1412 is therefore inhibition of FLJ20051 (Accession NM_019087). Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ20051. LOC221687 (Accession XM_166423) is another VGAM1412 host target gene. LOC221687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221687 BINDING SITE, designated SEQ ID:44302, to the nucleotide sequence of VGAM1412 RNA, herein designated VGAM RNA, also designated SEQ ID:4123.

[49355] Another function of VGAM1412 is therefore inhibition of LOC221687 (Accession XM_166423). Accordingly, utilities of VGAM1412 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221687. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1413 (VGAM1413) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49356] VGAM1413 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1413 was detected is described hereinabove with reference to Figs. 1–8.

[49357] VGAM1413 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Yellow Mosaic Virus. VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49358] VGAM1413 gene encodes a VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1413 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1413 precursor RNA is designated SEQ ID:1399, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1399 is located at position 4084 relative to the genome of Bean Yellow Mosaic Virus.

[49359] VGAM1413 precursor RNA folds onto itself, forming VGAM1413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49360] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1413 folded precursor RNA into VGAM1413 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1413 RNA is designated SEQ ID:4124, and is provided hereinbelow with reference to the sequence listing part.

[49361] VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1413 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49362] VGAM1413 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1413 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1413 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49363] The complementary binding of VGAM1413 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1413 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1413 host target RNA into VGAM1413 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49364] It is appreciated that VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1413 host target genes. The mRNA of each one of this plurality of VGAM1413 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1413 RNA, herein designated VGAM RNA, and which when bound by VGAM1413 RNA causes inhibition of translation of respective one or more VGAM1413 host target proteins.

[49365] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1413 gene, herein designated VGAM GENE, on one or more VGAM1413 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49366] It is yet further appreciated that a function of VGAM1413 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of viral infection by Bean Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1413 correlate with, and may be deduced from, the identity of the host target genes which VGAM1413 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49367] Nucleotide sequences of the VGAM1413 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1413 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1413 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1413 are further described hereinbelow with reference to Table 1.

[49368] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1413 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1413 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49369] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1413 gene, herein designated VGAM is inhibition of expression of VGAM1413 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1413 correlate with, and may be deduced from, the identity of the target genes which VGAM1413 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49370] Dyskeratosis Congenita 1, Dyskerin (DKC1, Accession NM_001363) is a VGAM1413 host target gene. DKC1 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by DKC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKC1 BINDING SITE, designated SEQ ID:7043, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49371] A function of VGAM1413 is therefore inhibition of Dyskeratosis Congenita 1, Dyskerin (DKC1, Accession NM_001363), a gene which may have cell cycle and nucleolar functions. Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKC1. The function of DKC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM559. Interleukin 16 (lymphocyte chemoattractant factor) (IL16, Accession NM_004513) is another VGAM1413 host target gene. IL16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of IL16 BINDING SITE, designated SEQ ID:10839, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49372] Another function of VGAM1413 is therefore inhibition of Interleukin 16 (lymphocyte chemoattractant factor) (IL16, Accession NM_004513), a gene which modulates T-cell activation. Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL16. The function of IL16 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM819. Cyclin B3 (CCNB3, Accession NM_033671) is another VGAM1413 host target gene. CCNB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNB3 BINDING SITE, designated SEQ ID:27396, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49373] Another function of VGAM1413 is therefore inhibition of Cyclin B3 (CCNB3, Accession NM_033671). Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNB3. DKFZP586M1120 (Accession NM_031294) is another VGAM1413 host target gene. DKFZP586M1120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586M1120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586M1120 BINDING SITE, designated SEQ ID:25317, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49374] Another function of VGAM1413 is therefore inhibition of DKFZP586M1120 (Accession NM_031294). Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586M1120. PB1 (Accession NM_018165) is another VGAM1413 host target gene. PB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PB1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PB1 BINDING SITE, designated SEQ ID:19978, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49375] Another function of VGAM1413 is therefore inhibition of PB1 (Accession NM_018165). Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PB1. Signal Recognition Particle 9kDa (SRP9, Accession XM_086431) is another VGAM1413 host target gene. SRP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRP9 BINDING SITE, designated SEQ ID:38649, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49376] Another function of VGAM1413 is therefore inhibition of Signal Recognition Particle 9kDa (SRP9, Accession XM_086431). Accordingly, utilities of VGAM1413 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with SRP9. LOC145268 (Accession XM_085072) is another VGAM1413 host target gene. LOC145268 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145268 BINDING SITE, designated SEQ ID:37812, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49377] Another function of VGAM1413 is therefore inhibition of LOC145268 (Accession XM_085072). Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145268. LOC153205 (Accession XM_098322) is another VGAM1413 host target gene. LOC153205 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153205 BINDING SITE, designated SEQ ID:41580, to the nucleotide sequence of VGAM1413 RNA, herein designated VGAM RNA, also designated SEQ ID:4124.

[49378] Another function of VGAM1413 is therefore inhibition of LOC153205 (Accession XM_098322). Accordingly, utilities of VGAM1413 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153205. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1414 (VGAM1414) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49379] VGAM1414 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1414 was detected is described hereinabove with reference to Figs. 1–8.

[49380] VGAM1414 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Yellow Mosaic Virus. VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49381] VGAM1414 gene encodes a VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1414 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1414 precursor RNA is designated SEQ ID:1400, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1400 is located at position 1603 relative to the genome of Bean Yellow Mosaic Virus.

[49382] VGAM1414 precursor RNA folds onto itself, forming VGAM1414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49383] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1414 folded precursor RNA into VGAM1414 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1414 RNA is designated SEQ ID:4125, and is provided hereinbelow with reference to the sequence listing part.

[49384] VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1414 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49385] VGAM1414 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1414 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1414 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49386] The complementary binding of VGAM1414 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1414 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1414 host target RNA into VGAM1414 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49387] It is appreciated that VGAM1414 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1414 host target genes. The mRNA of each one of this plurality of VGAM1414 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1414 RNA, herein designated VGAM RNA, and which when bound by VGAM1414 RNA causes inhibition of translation of respective one or more VGAM1414 host target proteins.

[49388] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1414 gene, herein designated VGAM GENE, on one or more VGAM1414 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[49389] It is yet further appreciated that a function of VGAM1414 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of viral infection by Bean Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1414 correlate with, and may be deduced from, the identity of the host target genes which VGAM1414 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49390] Nucleotide sequences of the VGAM1414 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1414 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1414 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1414 are further described hereinbelow with reference to Table 1.

[49391] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1414 host target RNA, and

schematic representation of the complementarity of each of these host target binding sites to VGAM1414 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49392] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1414 gene, herein designated VGAM is inhibition of expression of VGAM1414 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1414 correlate with, and may be deduced from, the identity of the target genes which VGAM1414 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49393] ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702) is a VGAM1414 host target gene. ATP1A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1A2 BINDING SITE, designated SEQ ID:6366, to the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, also designated SEQ ID:4125.

[49394] A function of VGAM1414 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Alpha 2 (+) Polypeptide (ATP1A2, Accession NM_000702). Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1A2. Proteoglycan 4, (megakaryocyte stimulating factor, articular superficial zone protein, camptodactyly, arthropathy, coxa vara, pericarditis syndrome) (PRG4, Accession NM_005807) is another VGAM1414 host target gene. PRG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRG4 BINDING SITE, designated SEQ ID:12383, to the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, also designated SEQ ID:4125.

[49395] Another function of VGAM1414 is therefore inhibition of Proteoglycan 4, (megakaryocyte stimulating factor, articular superficial zone protein, camptodactyly, arthropathy, coxa vara, pericarditis syndrome) (PRG4, Accession NM_005807). Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with PRG4. TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190) is another VGAM1414 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9181, to the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, also designated SEQ ID:4125.

[49396] Another function of VGAM1414 is therefore inhibition of TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAPBP. The function of TAPBP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM122.CEPT1 (Accession NM_006090) is another VGAM1414 host target gene. CEPT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by CEPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEPT1 BINDING SITE, designated SEQ ID:12737, to the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, also designated SEQ ID:4125.

[49397] Another function of VGAM1414 is therefore inhibition of CEPT1 (Accession NM_006090). Accordingly, utilities of VGAM1414 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEPT1. FLJ20086 (Accession NM_017661) is another VGAM1414 host target gene. FLJ20086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20086 BINDING SITE, designated SEQ ID:19190, to the nucleotide sequence of VGAM1414 RNA, herein designated VGAM RNA, also designated SEQ ID:4125.

[49398] Another function of VGAM1414 is therefore inhibition of FLJ20086 (Accession NM_017661). Accordingly, utilities of

VGAM1414 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20086. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1415 (VGAM1415) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49399] VGAM1415 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1415 was detected is described hereinabove with reference to Figs. 1–8.

[49400] VGAM1415 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Yellow Mosaic Virus. VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49401] VGAM1415 gene encodes a VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1415 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu–

cleotide sequence of VGAM1415 precursor RNA is designated SEQ ID:1401, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1401 is located at position 1048 relative to the genome of Bean Yellow Mosaic Virus.

[49402] VGAM1415 precursor RNA folds onto itself, forming VGAM1415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49403] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1415 folded precursor RNA into VGAM1415 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM1415 RNA is designated SEQ ID:4126, and

is provided hereinbelow with reference to the sequence listing part.

[49404] VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1415 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49405] VGAM1415 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1415 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1415 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49406] The complementary binding of VGAM1415 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1415 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1415 host target RNA into VGAM1415 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49407] It is appreciated that VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1415 host target genes. The mRNA of each one of this plurality of VGAM1415 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1415 RNA, herein designated VGAM RNA, and which when bound by VGAM1415 RNA causes inhibition of translation of respective one or more VGAM1415 host target proteins.

[49408] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1415 gene, herein designated VGAM GENE, on one or more VGAM1415 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49409] It is yet further appreciated that a function of VGAM1415 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1415 include diagnosis, prevention and treatment of viral infection by Bean Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1415 correlate with, and may be deduced from, the identity of the host target genes which VGAM1415 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49410] Nucleotide sequences of the VGAM1415 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1415 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1415 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1415 are further described hereinbelow with reference to Table 1.

[49411] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1415 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1415 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49412] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1415 gene, herein designated VGAM is inhibition of expression of VGAM1415 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1415 correlate with, and may be deduced from, the identity of the target genes which VGAM1415 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49413] DEK Oncogene (DNA binding) (DEK, Accession NM_003472) is a VGAM1415 host target gene. DEK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DEK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEK BINDING SITE, designated SEQ ID:9535, to the nucleotide sequence of VGAM1415 RNA, herein designated VGAM RNA, also designated SEQ ID:4126.

[49414] A function of VGAM1415 is therefore inhibition of DEK Oncogene (DNA binding) (DEK, Accession NM_003472), a gene which interacts in transcriptional regulation and signal transduction. Accordingly, utilities of VGAM1415 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEK. The function of

DEK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795.FLJ31300 (Accession NM_144639) is another VGAM1415 host target gene. FLJ31300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31300 BINDING SITE, designated SEQ ID:29461, to the nucleotide sequence of VGAM1415 RNA, herein designated VGAM RNA, also designated SEQ ID:4126.

[49415] Another function of VGAM1415 is therefore inhibition of FLJ31300 (Accession NM_144639). Accordingly, utilities of VGAM1415 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31300. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1416 (VGAM1416) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[49416] VGAM1416 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1416 was detected is described hereinabove with reference to Figs. 1–8.

[49417] VGAM1416 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ryegrass Mosaic Virus. VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49418] VGAM1416 gene encodes a VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1416 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1416 precursor RNA is designated SEQ ID:1402, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1402 is located at position 4175 relative to the genome of Ryegrass Mosaic Virus.

[49419] VGAM1416 precursor RNA folds onto itself, forming VGAM1416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49420] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1416 folded precursor RNA into VGAM1416 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1416 RNA is designated SEQ ID:4127, and is provided hereinbelow with reference to the sequence listing part.

[49421] VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1416 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49422] VGAM1416 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1416 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1416 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[49423] The complementary binding of VGAM1416 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1416 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1416 host target RNA into VGAM1416 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49424] It is appreciated that VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1416 host target genes. The mRNA of each one of this plurality of VGAM1416 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1416 RNA, herein designated VGAM RNA, and which when bound by VGAM1416 RNA causes inhibition of translation of respective one or more VGAM1416 host target proteins.

[49425] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1416 gene, herein designated VGAM GENE, on one

or more VGAM1416 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49426] It is yet further appreciated that a function of VGAM1416 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of viral infection by Ryegrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1416 correlate with, and may be deduced from, the identity of the host target genes which VGAM1416 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49427] Nucleotide sequences of the VGAM1416 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1416 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1416 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1416 are further described hereinbelow with reference to Table 1.

[49428] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1416 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1416 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49429] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1416 gene, herein designated VGAM is inhibition of expression of VGAM1416 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1416 correlate with, and may be deduced from, the identity of the target genes which VGAM1416 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49430] Dentin Matrix Acidic Phosphoprotein (DMP1, Accession

NM_004407) is a VGAM1416 host target gene. DMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMP1 BINDING SITE, designated SEQ ID:10660, to the nucleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, also designated SEQ ID:4127.

[49431] A function of VGAM1416 is therefore inhibition of Dentin Matrix Acidic Phosphoprotein (DMP1, Accession NM_004407), a gene which regulates mineralization of bone and dentin. Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMP1. The function of DMP1 has been established by previous studies. George et al. (1993) isolated a dentin matrix acidic phosphoprotein from a rat odontoblast cDNA library. It is a serine-rich acidic protein that has numerous potential phosphorylation sites, especially for messenger-independent kinases of the casein kinase II group. Expression analysis showed that dmp1 message is essentially dentin-specific. The mouse dmp1 gene was mapped to 5q21, a region of the

mouse genome that shows homology of synteny with human 4q21. Dentinogenesis imperfecta type II (OMIM Ref. No. 125490) maps to that region of the genome, namely 4q13–q21. This prompted Aplin et al. (1995) to isolate a cosmid containing the human DMP1 gene. The isolation of a short tandem repeat polymorphism at this locus allowed them to map DMP1 to 4q21 and demonstrate that it is tightly linked to DGI1 in 2 families. The creation of a YAC contig around the gene for osteopontin (OMIM Ref. No. 166490) allowed them to demonstrate that DMP1 is located within 150 kb of the bone sialoprotein locus (OMIM Ref. No. 147563) and within 490 kb of the SPP1 locus. Mutation search in both SPP1 and IBSP in individuals with dentinogenesis imperfecta yielded negative results. DMP1 is a candidate for similar mutation screen. MacDougall et al. (1996) used fluorescence in situ hybridization to map DMP1 to 4q21. By screening a cDNA library constructed from mandibular and maxillary third molars with the mouse *Dmp1* sequence as the probe, Hirst et al. (1997) isolated a cDNA encoding DMP1. The deduced 513–amino acid, highly acidic, serine–rich protein has a hydrophobic signal peptide, an Arg–Gly–Asp cell–attachment sequence, and numerous potential serine phosphorylation sites. Ge–

omic sequence analysis indicated that the DMP1 gene contains 6 exons, and no disease-specific mutations were identified in 2 families with type II dentinogenesis imperfecta.

[49432] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49433] Hirst, K. L.; Simmons, D.; Feng, J.; Aplin, H.; Dixon, M. J.; MacDougall, M. : Elucidation of the sequence and the genomic organization of the human dentin matrix acidic phosphoprotein 1 (DMP1) gene: exclusion of the locus from a causative role in the pathogenesis of dentinogenesis imperfecta type II. *Genomics* 42: 38–45, 1997. ; and

[49434] MacDougall, M.; DuPont, B. R.; Simmons, D.; Leach, R. J. : Assignment of DMP1 to human chromosome 4 band q21 by in situ hybridization. *Cytogenet. Cell. Genet.* 74: 189 only, 1996.

[49435] Further studies establishing the function and utilities of DMP1 are found in John Hopkins OMIM database record ID 600980, and in cited publications numbered 12524–7809 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. E74-like Factor 2 (ets domain transcription factor) (ELF2, Accession

NM_006874) is another VGAM1416 host target gene. ELF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELF2 BINDING SITE, designated SEQ ID:13742, to the nucleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, also designated SEQ ID:4127.

[49436] Another function of VGAM1416 is therefore inhibition of E74-like Factor 2 (ets domain transcription factor) (ELF2, Accession NM_006874). Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELF2. KIAA1586 (Accession XM_166451) is another VGAM1416 host target gene. KIAA1586 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1586, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1586 BINDING SITE, designated SEQ ID:44347, to the nucleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4127.

[49437] Another function of VGAM1416 is therefore inhibition of KIAA1586 (Accession XM_166451). Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1586. Mab-21-like 2 (C. elegans) (MAB21L2, Accession NM_006439) is another VGAM1416 host target gene. MAB21L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAB21L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L2 BINDING SITE, designated SEQ ID:13148, to the nucleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, also designated SEQ ID:4127.

[49438] Another function of VGAM1416 is therefore inhibition of Mab-21-like 2 (C. elegans) (MAB21L2, Accession NM_006439). Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L2. Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM_031988) is another VGAM1416 host target gene.

MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP2K6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2, designated SEQ ID:25700 and SEQ ID:8640 respectively, to the nucleotide sequence of VGAM1416 RNA, herein designated VGAM RNA, also designated SEQ ID:4127.

[49439] Another function of VGAM1416 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM_031988). Accordingly, utilities of VGAM1416 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K6. KIAA0907 (Accession NM_014949) is another VGAM1417 host target gene. KIAA0907 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0907, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0907 BINDING SITE, designated SEQ ID:17278, to the nucleotide sequence of VGAM1417

RNA, herein designated VGAM RNA, also designated SEQ ID:4128.

[49440] Another function of VGAM1417 is therefore inhibition of KIAA0907 (Accession NM_014949). Accordingly, utilities of VGAM1417 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0907. LOC219722 (Accession XM_167593) is another VGAM1417 host target gene. LOC219722 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219722, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219722 BINDING SITE, designated SEQ ID:44711, to the nucleotide sequence of VGAM1417 RNA, herein designated VGAM RNA, also designated SEQ ID:4128.

[49441] Another function of VGAM1417 is therefore inhibition of LOC219722 (Accession XM_167593). Accordingly, utilities of VGAM1417 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219722. LOC256113 (Accession XM_172989) is another VGAM1417 host target gene. LOC256113 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC256113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256113 BINDING SITE, designated SEQ ID:46261, to the nucleotide sequence of VGAM1417 RNA, herein designated VGAM RNA, also designated SEQ ID:4128.

[49442] Another function of VGAM1417 is therefore inhibition of LOC256113 (Accession XM_172989). Accordingly, utilities of VGAM1417 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256113. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1418 (VGAM1418) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49443] VGAM1418 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1418 was detected is described hereinabove with reference to Figs. 1-8.

[49444] VGAM1418 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Ryegrass Mosaic Virus. VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49445] VGAM1418 gene encodes a VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1418 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1418 precursor RNA is designated SEQ ID:1404, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1404 is located at position 3047 relative to the genome of Ryegrass Mosaic Virus.

[49446] VGAM1418 precursor RNA folds onto itself, forming VGAM1418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49447] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1418 folded precursor RNA into VGAM1418 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1418 RNA is designated SEQ ID:4129, and is provided hereinbelow with reference to the sequence listing part.

[49448] VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1418 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49449] VGAM1418 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1418 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1418 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49450] The complementary binding of VGAM1418 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1418 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1418

host target RNA into VGAM1418 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49451] It is appreciated that VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1418 host target genes. The mRNA of each one of this plurality of VGAM1418 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1418 RNA, herein designated VGAM RNA, and which when bound by VGAM1418 RNA causes inhibition of translation of respective one or more VGAM1418 host target proteins.

[49452] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1418 gene, herein designated VGAM GENE, on one or more VGAM1418 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49453] It is yet further appreciated that a function of VGAM1418 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1418 include diagnosis, prevention and treatment of viral infection by Ryegrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1418 correlate with, and may be deduced from, the identity of the host target genes which VGAM1418 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49454] Nucleotide sequences of the VGAM1418 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1418 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1418 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1418 are further

described hereinbelow with reference to Table 1.

[49455] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1418 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1418 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49456] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1418 gene, herein designated VGAM is inhibition of expression of VGAM1418 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1418 correlate with, and may be deduced from, the identity of the target genes which VGAM1418 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49457] FLJ12409 (Accession NM_025105) is a VGAM1418 host target gene. FLJ12409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12409 BINDING SITE,

designated SEQ ID:24751, to the nucleotide sequence of VGAM1418 RNA, herein designated VGAM RNA, also designated SEQ ID:4129.

[49458] A function of VGAM1418 is therefore inhibition of FLJ12409 (Accession NM_025105). Accordingly, utilities of VGAM1418 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12409. LOC115442 (Accession XM_052510) is another VGAM1418 host target gene. LOC115442 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115442, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115442 BINDING SITE, designated SEQ ID:35981, to the nucleotide sequence of VGAM1418 RNA, herein designated VGAM RNA, also designated SEQ ID:4129.

[49459] Another function of VGAM1418 is therefore inhibition of LOC115442 (Accession XM_052510). Accordingly, utilities of VGAM1418 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115442. LOC196074 (Accession XM_113647) is another VGAM1418 host target gene. LOC196074 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196074 BINDING SITE, designated SEQ ID:42322, to the nucleotide sequence of VGAM1418 RNA, herein designated VGAM RNA, also designated SEQ ID:4129.

[49460] Another function of VGAM1418 is therefore inhibition of LOC196074 (Accession XM_113647). Accordingly, utilities of VGAM1418 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196074. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1419 (VGAM1419) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49461] VGAM1419 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1419 was detected is described hereinabove with reference to Figs. 1-8.

[49462] VGAM1419 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ryegrass Mosaic Virus. VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49463] VGAM1419 gene encodes a VGAM1419 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1419 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1419 precursor RNA is designated SEQ ID:1405, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1405 is located at position 4295 relative to the genome of Ryegrass Mosaic Virus.

[49464] VGAM1419 precursor RNA folds onto itself, forming VGAM1419 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[49465] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1419 folded precursor RNA into VGAM1419 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1419 RNA is designated SEQ ID:4130, and is provided hereinbelow with reference to the sequence listing part.

[49466] VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1419 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49467] VGAM1419 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1419 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1419 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1419 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49468] The complementary binding of VGAM1419 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1419 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1419 host target RNA into VGAM1419 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49469] It is appreciated that VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1419 host target genes. The mRNA of each one of this plurality of VGAM1419 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1419 RNA, herein designated VGAM RNA, and which when bound by VGAM1419 RNA causes inhibition of translation of respective one or more VGAM1419 host target proteins.

[49470] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1419 gene, herein designated VGAM GENE, on one or more VGAM1419 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49471] It is yet further appreciated that a function of VGAM1419 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of viral infection by Ryegrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1419 correlate with, and may be deduced from, the identity of the host target genes which VGAM1419 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49472] Nucleotide sequences of the VGAM1419 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1419 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1419 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1419 are further described hereinbelow with reference to Table 1.

[49473] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1419 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1419 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49474] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1419 gene, herein designated VGAM is inhibition of expression of VGAM1419 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1419 correlate with, and may be deduced from, the identity of the target genes which VGAM1419 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49475] Acidic Repeat Containing (ACRC, Accession NM_052957) is a VGAM1419 host target gene. ACRC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACRC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ACRC BINDING SITE, designated SEQ ID:27518, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49476] A function of VGAM1419 is therefore inhibition of Acidic Repeat Containing (ACRC, Accession NM_052957). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACRC. Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357) is another VGAM1419 host target gene. CASP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP8 BINDING SITE, designated SEQ ID:27207, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49477] Another function of VGAM1419 is therefore inhibition of Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_033357), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor

and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM145. Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269) is another VGAM1419 host target gene. NR2E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR2E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR2E1 BINDING SITE, designated SEQ ID:9281, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49478] Another function of VGAM1419 is therefore inhibition of Nuclear Receptor Subfamily 2, Group E, Member 1 (NR2E1, Accession NM_003269), a gene which may be required for brain development and be involved in the regulation of retinal development . Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with NR2E1. The function of NR2E1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM689. Vanin 1 (VNN1, Accession NM_004666) is another VGAM1419 host target gene. VNN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VNN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VNN1 BINDING SITE, designated SEQ ID:11041, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49479] Another function of VGAM1419 is therefore inhibition of Vanin 1 (VNN1, Accession NM_004666), a gene which may regulate steps in thymus homing and play a role in mammalian sexual development. Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VNN1. The function of VNN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM419. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375) is another VGAM1419 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33514, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49480] Another function of VGAM1419 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM_004367) is another VGAM1419 host target gene. CCR6 BINDING SITE1 and CCR6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of CCR6 BINDING SITE1 and CCR6 BINDING SITE2, designated SEQ ID:10580 and SEQ ID:25374 respectively, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49481] Another function of VGAM1419 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM_004367). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. Olfactory Receptor, Family 2, Subfamily C, Member 3 (OR2C3, Accession XM_060575) is another VGAM1419 host target gene. OR2C3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OR2C3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OR2C3 BINDING SITE, designated SEQ ID:37177, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49482] Another function of VGAM1419 is therefore inhibition of Olfactory Receptor, Family 2, Subfamily C, Member 3 (OR2C3, Accession XM_060575). Accordingly, utilities of

VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OR2C3. RI58 (Accession NM_012420) is another VGAM1419 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RI58, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ ID:14798, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49483] Another function of VGAM1419 is therefore inhibition of RI58 (Accession NM_012420). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. Testis Expressed Sequence 27 (TEX27, Accession NM_021943) is another VGAM1419 host target gene. TEX27 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEX27, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of TEX27 BINDING SITE, designated SEQ ID:22462, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49484] Another function of VGAM1419 is therefore inhibition of Testis Expressed Sequence 27 (TEX27, Accession NM_021943). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEX27. LOC123036 (Accession XM_058676) is another VGAM1419 host target gene. LOC123036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC123036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123036 BINDING SITE, designated SEQ ID:36718, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49485] Another function of VGAM1419 is therefore inhibition of LOC123036 (Accession XM_058676). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC123036. LOC221773 (Accession XM_165802) is another VGAM1419 host target gene. LOC221773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221773 BINDING SITE, designated SEQ ID:43768, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49486] Another function of VGAM1419 is therefore inhibition of LOC221773 (Accession XM_165802). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221773. LOC253584 (Accession XM_173068) is another VGAM1419 host target gene. LOC253584 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253584 BINDING SITE, designated SEQ ID:46322, to the nucleotide sequence of VGAM1419 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4130.

[49487] Another function of VGAM1419 is therefore inhibition of LOC253584 (Accession XM_173068). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253584. LOC253912 (Accession XM_173222) is another VGAM1419 host target gene. LOC253912 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253912 BINDING SITE, designated SEQ ID:46484, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49488] Another function of VGAM1419 is therefore inhibition of LOC253912 (Accession XM_173222). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253912. LOC51185 (Accession NM_016302) is another VGAM1419 host target gene. LOC51185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51185, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51185 BINDING SITE, designated SEQ ID:18425, to the nucleotide sequence of VGAM1419 RNA, herein designated VGAM RNA, also designated SEQ ID:4130.

[49489] Another function of VGAM1419 is therefore inhibition of LOC51185 (Accession NM_016302). Accordingly, utilities of VGAM1419 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51185. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1420 (VGAM1420) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49490] VGAM1420 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1420 was detected is described hereinabove with reference to Figs. 1-8.

[49491] VGAM1420 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Hepatitis GB Virus A.

VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49492] VGAM1420 gene encodes a VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1420 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1420 precursor RNA is designated SEQ ID:1406, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1406 is located at position 4594 relative to the genome of Hepatitis GB Virus A.

[49493] VGAM1420 precursor RNA folds onto itself, forming VGAM1420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49494] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1420 folded precursor RNA into VGAM1420 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1420 RNA is designated SEQ ID:4131, and is provided hereinbelow with reference to the sequence listing part.

[49495] VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1420 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49496] VGAM1420 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1420 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1420 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49497] The complementary binding of VGAM1420 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1420 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1420 host target RNA into VGAM1420 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49498] It is appreciated that VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1420 host target genes. The mRNA of each one of this plurality of VGAM1420 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1420 RNA, herein designated VGAM RNA, and which when bound by VGAM1420 RNA causes inhibition of translation of respective one or more VGAM1420 host target proteins.

[49499] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1420 gene, herein designated VGAM GENE, on one or more VGAM1420 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49500] It is yet further appreciated that a function of VGAM1420 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus A. Specific functions, and accordingly utilities, of VGAM1420 correlate with, and may be deduced from, the identity of the host target genes which VGAM1420 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49501] Nucleotide sequences of the VGAM1420 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1420 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1420 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1420 are further described hereinbelow with reference to Table 1.

[49502] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1420 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1420 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49503] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1420 gene, herein designated VGAM is inhibition of expression of VGAM1420 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1420 correlate with, and may be deduced from, the identity of the target genes which VGAM1420 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49504] Caspase 7, Apoptosis-related Cysteine Protease (CASP7, Accession NM_001227) is a VGAM1420 host target gene. CASP7 BINDING SITE1 through CASP7 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP7 BINDING SITE1

through CASP7 BINDING SITE4, designated SEQ ID:6895, SEQ ID:27191, SEQ ID:27192 and SEQ ID:27193 respectively, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49505] A function of VGAM1420 is therefore inhibition of Caspase 7, Apoptosis-related Cysteine Protease (CASP7, Accession NM_001227), a gene which is an apoptosis-related caspase and involves in the activation of executing caspases. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP7. The function of CASP7 has been established by previous studies. Fernandes-Alnemri et al. (1995) found that active MCH3-alpha protein is made by the cleavage of pro-MCH3-alpha into 2 subunits, p20 and p12. Active CPP32 is similarly made by cleavage of its precursor, pro-CPP32, into 2 subunits. They found that CPP32 could cleave pro-MCH3-alpha into its subunits, but that MCH3-alpha could not cleave pro-CPP32. The authors further demonstrated that MCH4 (OMIM Ref. No. 601762) can cleave pro-MCH3 into its 2 subunits (Fernandes-Alnemri et al., 1996). Expression of MCH3-alpha/CPP32 heterodimers in Sf9 cells induced

apoptosis. They also found that MCH3 cleaves poly(ADP-ribose) polymerase (PARP) with similar kinetics to that of CPP32. Thus Fernandes-Alnemri et al. (1995) concluded that the cleavage of PARP during apoptosis cannot solely be attributed to CPP32 but could also be an activity of its closely related homolog, MCH3-alpha. Riedl et al. (2001) crystallized the C285A variant of human pro-caspase-7 and solved its crystal structure at 2.9 angstrom. Analysis of this executioner zymogen structure and its comparison with the structures of active caspase-7 unveiled the structural basis of the procaspase inactivity and suggested the conformational changes leading to procaspase activation.

[49506] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49507] Fernandes-Alnemri, T.; Armstrong, R. C.; Krebs, J.; Srinivasula, S. M.; Wang, L.; Bullrich, F.; Fritz, L. C.; Trapani, J. A.; Tomaselli, K. J.; Litwack, G.; Alnemri, E. S. : In vitro activation of CPP32 and Mch3 by Mch4, a novel human apoptotic cysteine protease containing two FADD-like domains. Proc. Nat. Acad. Sci. 93: 7464-7469, 1996. ; and

[49508] Riedl, S. J.; Fuentes-Prior, P.; Renatus, M.; Kairies, N.;

Krapp, S.; Huber, R.; Salvesen, G. S.; Bode, W. : Structural basis for the activation of human procaspase-7. Proc. Nat. Acad. S.

[49509] Further studies establishing the function and utilities of CASP7 are found in John Hopkins OMIM database record ID 601761, and in cited publications numbered 6710, 7119-671 and 7126 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. G Protein-coupled Receptor 81 (GPR81, Accession NM_032554) is another VGAM1420 host target gene. GPR81 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR81, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR81 BINDING SITE, designated SEQ ID:26277, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49510] Another function of VGAM1420 is therefore inhibition of G Protein-coupled Receptor 81 (GPR81, Accession NM_032554). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with GPR81. Heat Shock 60kDa Protein 1 (chaperonin) (HSPD1, Accession XM_012182) is another VGAM1420 host target gene. HSPD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPD1 BINDING SITE, designated SEQ ID:30207, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49511] Another function of VGAM1420 is therefore inhibition of Heat Shock 60kDa Protein 1 (chaperonin) (HSPD1, Accession XM_012182), a gene which is implicated in mitochondrial protein import and macromolecular assembly. may facilitate the correct folding of imported proteins. may also prevent misfolding and promote the refolding and proper assembly of unfolded polypeptides generated under stress conditions in the mitochondrial matrix. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPD1. The function of HSPD1 and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM1173. Oxysterol Binding Protein (OSBP, Accession NM_002556) is another VGAM1420 host target gene. OSBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OSBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBP BINDING SITE, designated SEQ ID:8407, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49512] Another function of VGAM1420 is therefore inhibition of Oxysterol Binding Protein (OSBP, Accession NM_002556). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBP. Placental Growth Factor, Vascular Endothelial Growth Factor-related Protein (PGF, Accession NM_002632) is another VGAM1420 host target gene. PGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PGF BINDING SITE, designated SEQ ID:8491, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49513] Another function of VGAM1420 is therefore inhibition of Placental Growth Factor, Vascular Endothelial Growth Factor-related Protein (PGF, Accession NM_002632), a gene which is a growth factor active in angiogenesis, and endothelial cell growth, stimulating cell proliferation and migration. it binds to receptor vegfr-1/fl. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGF. The function of PGF has been established by previous studies. Angiogenesis is a crucial process during development, certain periods of adult life, and tumorigenesis, and is tightly regulated by a network of growth factors and growth factor receptors. Maglione et al. (1991) isolated a human cDNA encoding a protein related to the vascular permeability factor (VPF; also VEGF; 192240). The protein, symbolized PLGF by them, is 149 amino acids long and shares 53% identity with the platelet-derived growth factor-like region of human VPF. They showed that the N-glycosylated PLGF protein is secreted into the

medium and that it functions as a dimer Animal model experiments lend further support to the function of PGF. Carmeliet et al. (2001) developed Pgf-deficient mice by targeted disruption. Pgf $-/-$ mice were born at expected mendelian ratios and were viable and fertile. Pgf $-/-$ mice had subtle changes of VEGF-dependent retinal and luteal angiogenesis. Pgf $-/-$ mice manifested impaired angiogenesis, plasma extravasation, and collateral growth during ischemia, inflammation, wound healing, and cancer. Transplantation of wildtype bone marrow rescued the impaired angiogenesis and collateral growth in Pgf $-/-$ mice, indicating that PGF might have contributed to vessel growth in the adult by mobilizing bone marrow-derived cells. The synergism between PGF and VEGF was specific, as PGF deficiency impaired the response to VEGF, but not to FGF (OMIM Ref. No. 131220) or histamine. VEGFR1 was activated by PGF, given that anti-VEGFR1 antibodies and a Src-kinase inhibitor blocked the endothelial response to PGF or VEGF/PLGF. By upregulating PGF and the signaling subtype of VEGFR1, endothelial cells amplify their responsiveness to VEGF during the 'angiogenic switch' in many pathologic disorders

[49514] It is appreciated that the abovementioned animal model

for PGF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[49515] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49516] Maglione, D.; Guerriero, V.; Viglietto, G.; Delli-Bovi, P.; Persico, M. G. : Isolation of a human placenta cDNA coding for a protein related to the vascular permeability factor. Proc. Nat. Acad. Sci. 88: 9267-9271, 1991. ; and

[49517] Carmeliet, P.; Moons, L.; Luttun, A.; Vincenti, V.; Compernelle, V.; De Mol, M.; Wu, Y.; Bono, F.; Devy, L.; Beck, H.; Scholz, D.; Acker, T.; and 17 others : Synergism between vascular endo.

[49518] Further studies establishing the function and utilities of PGF are found in John Hopkins OMIM database record ID 601121, and in cited publications numbered 6366-6369 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Very Low Density Lipoprotein Receptor (VLDLR, Accession XM_045386) is another VGAM1420 host target gene. VLDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VLDLR, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VLDLR BINDING SITE, designated SEQ ID:34448, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49519] Another function of VGAM1420 is therefore inhibition of Very Low Density Lipoprotein Receptor (VLDLR, Accession XM_045386), a gene which may play a crucial role in triglyceride metabolism. Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VLDLR. The function of VLDLR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM103. Aminocarboxymuconate Semialdehyde Decarboxylase (acmsd, Accession NM_138326) is another VGAM1420 host target gene. acmsd BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by acmsd, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of acmsd BINDING SITE,

designated SEQ ID:28727, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49520] Another function of VGAM1420 is therefore inhibition of Aminocarboxymuconate Semialdehyde Decarboxylase (acmsd, Accession NM_138326). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with acmsd. A Disintegrin and Metalloproteinase Domain 9 (meltrin gamma) (ADAM9, Accession NM_003816) is another VGAM1420 host target gene. ADAM9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM9 BINDING SITE, designated SEQ ID:9904, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49521] Another function of VGAM1420 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 9 (meltrin gamma) (ADAM9, Accession NM_003816). Accordingly, utilities of VGAM1420 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with ADAM9. UDP-Gal:betaGal Beta 1,3-galactosyltransferase Polypeptide 6 (B3GALT6, Accession NM_080605) is another VGAM1420 host target gene. B3GALT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B3GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT6 BINDING SITE, designated SEQ ID:27922, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49522] Another function of VGAM1420 is therefore inhibition of UDP-Gal:betaGal Beta 1,3-galactosyltransferase Polypeptide 6 (B3GALT6, Accession NM_080605). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT6. BC008967 (Accession XM_027309) is another VGAM1420 host target gene. BC008967 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BC008967, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BC008967 BINDING SITE, designated SEQ ID:30477, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49523] Another function of VGAM1420 is therefore inhibition of BC008967 (Accession XM_027309). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BC008967. CL683 (Accession NM_015696) is another VGAM1420 host target gene. CL683 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CL683, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CL683 BINDING SITE, designated SEQ ID:17923, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49524] Another function of VGAM1420 is therefore inhibition of CL683 (Accession NM_015696). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CL683.

FLJ14596 (Accession NM_032809) is another VGAM1420 host target gene. FLJ14596 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14596 BINDING SITE, designated SEQ ID:26571, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49525] Another function of VGAM1420 is therefore inhibition of FLJ14596 (Accession NM_032809). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14596. Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM_133443) is another VGAM1420 host target gene. GPT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPT2 BINDING SITE, designated SEQ ID:28525, to the nucleotide se-

quence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49526] Another function of VGAM1420 is therefore inhibition of Glutamic Pyruvate Transaminase (alanine aminotransferase) 2 (GPT2, Accession NM_133443). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPT2. KIAA0020 (Accession NM_014878) is another VGAM1420 host target gene. KIAA0020 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0020 BINDING SITE, designated SEQ ID:17020, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49527] Another function of VGAM1420 is therefore inhibition of KIAA0020 (Accession NM_014878). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0020. KIAA0766 (Accession NM_014805) is another VGAM1420 host target gene. KIAA0766 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0766 BINDING SITE, designated SEQ ID:16739, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49528] Another function of VGAM1420 is therefore inhibition of KIAA0766 (Accession NM_014805). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0766. KIAA0864 (Accession XM_032630) is another VGAM1420 host target gene. KIAA0864 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0864, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0864 BINDING SITE, designated SEQ ID:31685, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49529] Another function of VGAM1420 is therefore inhibition of

KIAA0864 (Accession XM_032630). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0864. KIAA1344 (Accession XM_051699) is another VGAM1420 host target gene. KIAA1344 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1344, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1344 BINDING SITE, designated SEQ ID:35871, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49530] Another function of VGAM1420 is therefore inhibition of KIAA1344 (Accession XM_051699). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1344. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1420 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12798, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49531] Another function of VGAM1420 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622) is another VGAM1420 host target gene. MRPL35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL35 BINDING SITE, designated SEQ ID:18737, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49532] Another function of VGAM1420 is therefore inhibition of Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622). Accordingly, utilities of VGAM1420 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL35. PURG (Accession NM_013357) is another VGAM1420 host target gene.

PURG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PURG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PURG BINDING SITE, designated SEQ ID:15006, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49533] Another function of VGAM1420 is therefore inhibition of PURG (Accession NM_013357). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PURG. Rho-related BTB Domain Containing 1 (RHOBTB1, Accession XM_166144) is another VGAM1420 host target gene. RHOBTB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RHOBTB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB1 BINDING SITE, designated SEQ

ID:43949, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49534] Another function of VGAM1420 is therefore inhibition of Rho-related BTB Domain Containing 1 (RHOBTB1, Accession XM_166144). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB1. Vacuolar Protein Sorting 4B (yeast) (VPS4B, Accession NM_004869) is another VGAM1420 host target gene. VPS4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS4B BINDING SITE, designated SEQ ID:11292, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49535] Another function of VGAM1420 is therefore inhibition of Vacuolar Protein Sorting 4B (yeast) (VPS4B, Accession NM_004869). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS4B. LOC150397

(Accession XM_086907) is another VGAM1420 host target gene. LOC150397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150397 BINDING SITE, designated SEQ ID:38956, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49536] Another function of VGAM1420 is therefore inhibition of LOC150397 (Accession XM_086907). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150397. LOC199221 (Accession XM_087310) is another VGAM1420 host target gene. LOC199221 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199221 BINDING SITE, designated SEQ ID:39164, to the nucleotide sequence of VGAM1420 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4131.

[49537] Another function of VGAM1420 is therefore inhibition of LOC199221 (Accession XM_087310). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199221. LOC221688 (Accession XM_168085) is another VGAM1420 host target gene. LOC221688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221688 BINDING SITE, designated SEQ ID:44989, to the nucleotide sequence of VGAM1420 RNA, herein designated VGAM RNA, also designated SEQ ID:4131.

[49538] Another function of VGAM1420 is therefore inhibition of LOC221688 (Accession XM_168085). Accordingly, utilities of VGAM1420 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221688. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1421 (VGAM1421) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49539] VGAM1421 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1421 was detected is described hereinabove with reference to Figs. 1–8.

[49540] VGAM1421 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Hepatitis GB Virus A. VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49541] VGAM1421 gene encodes a VGAM1421 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1421 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1421 precursor RNA is designated SEQ ID:1407, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1407 is located at position 2844 relative to the genome of Hepatitis GB Virus A.

[49542] VGAM1421 precursor RNA folds onto itself, forming

VGAM1421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49543] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1421 folded precursor RNA into VGAM1421 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1421 RNA is designated SEQ ID:4132, and is provided hereinbelow with reference to the sequence listing part.

[49544] VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1421 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[49545] VGAM1421 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1421 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1421 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49546] The complementary binding of VGAM1421 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1421 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1421 host target RNA into VGAM1421 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49547] It is appreciated that VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1421 host target genes. The mRNA of each one of this plurality of VGAM1421 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1421 RNA, herein designated VGAM RNA, and which when bound by VGAM1421 RNA causes inhibition of translation of respective one or more VGAM1421 host target proteins.

[49548] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1421 gene, herein designated VGAM GENE, on one or more VGAM1421 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49549] It is yet further appreciated that a function of VGAM1421 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus A. Specific functions, and accordingly utilities, of VGAM1421 correlate with, and may be deduced from, the identity of the host target genes which VGAM1421 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[49550] Nucleotide sequences of the VGAM1421 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1421 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1421 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1421 are further described hereinbelow with reference to Table 1.

[49551] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1421 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1421 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49552] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1421 gene, herein designated VGAM is inhibition of expression of VGAM1421 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1421 correlate with, and may be deduced from, the identity of the target genes which VGAM1421 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[49553] CD28 Antigen (Tp44) (CD28, Accession NM_006139) is a VGAM1421 host target gene. CD28 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CD28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD28 BINDING SITE, designated SEQ ID:12781, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49554] A function of VGAM1421 is therefore inhibition of CD28 Antigen (Tp44) (CD28, Accession NM_006139), a gene which possibly involved in t-cell activation. Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD28. The function of CD28 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM281. Desmoglein 1 (DSG1, Accession NM_001942) is another VGAM1421 host target gene. DSG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DSG1,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSG1 BINDING SITE, designated SEQ ID:7656, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49555] Another function of VGAM1421 is therefore inhibition of Desmoglein 1 (DSG1, Accession NM_001942). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSG1. Heterogeneous Nuclear Ribonucleoprotein A1 (HNRPA1, Accession NM_031157) is another VGAM1421 host target gene. HNRPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPA1 BINDING SITE, designated SEQ ID:25247, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49556] Another function of VGAM1421 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein A1 (HNRPA1,

Accession NM_031157), a gene which involves in the packaging of pre-mrna into hnnp particles, transportes mRNA from the nucleus to the cytoplasm. Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPA1. The function of HNRPA1 has been established by previous studies. See 164020. In eukaryotic cells, nascent RNA polymerase II transcripts are associated in the nucleus with specific proteins to form ribonucleo-protein complexes called HNRP or 40S. Protein moiety of the 40S particle has 6 major components called core proteins, A1/A2, B1/B2, and C1/C2, plus a number of other proteins. Buoli et al. (1988) isolated and sequenced the cDNA for human HNRPA1. Southern analysis showed that HNRPA1-specific sequences are present in the human genome as a multigene family of about 30 members, most of them corresponding to pseudogenes of the processed type. Biamonti et al. (1989) succeeded in isolating an active HNRPA1 gene which was split into 10 exons and was 4.6 kb long. Michael et al. (1995) reported that HNRPA1 shuttles continuously between the nucleus and cytoplasm and contains a 38-amino acid domain, termed M9, that acts as both a nuclear localization and nuclear export sig-

nal. They suggested that HNRPA1 and other shuttling hn-RNPs function as carriers for RNA during export to the cytoplasm.

[49557] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49558] Biamonti, G.; Buvoli, M.; Bassi, M. T.; Morandi, C.; Cobianchi, F.; Riva, S. : Isolation of an active gene encoding human hnRNP protein A1: evidence for alternative splicing. *J. Molec. Biol.* 207: 491–503, 1989. ; and

[49559] Michael, W. M.; Choi, M.; Dreyfuss, G. : A nuclear export signal in hnRNP A1: a signal-mediated, temperature-dependent nuclear protein export pathway. *Cell* 83: 415–422, 1995.

[49560] Further studies establishing the function and utilities of HNRPA1 are found in John Hopkins OMIM database record ID 164017, and in cited publications numbered 1719–172 and 1723 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. V-myc Myelocytomatosis Viral Oncogene Homolog 2 (avian) (MYCL2, Accession NM_005377) is another VGAM1421 host target gene. MYCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by MYCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCL2 BINDING SITE, designated SEQ ID:11856, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49561] Another function of VGAM1421 is therefore inhibition of V-myc Myelocytomatosis Viral Oncogene Homolog 2 (avian) (MYCL2, Accession NM_005377). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCL2. PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746) is another VGAM1421 host target gene. PCTK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCTK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTK3 BINDING SITE, designated SEQ ID:36125, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49562] Another function of VGAM1421 is therefore inhibition of PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746), a gene which may play a role in signal transduction cascades in terminally differentiated cells. Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCTK3. The function of PCTK3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132. SRGAP2 (Accession XM_059095) is another VGAM1421 host target gene. SRGAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRGAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRGAP2 BINDING SITE, designated SEQ ID:36880, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49563] Another function of VGAM1421 is therefore inhibition of SRGAP2 (Accession XM_059095). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SR-GAP2. Chromosome 11 Open Reading Frame 9 (C11orf9, Accession NM_013279) is another VGAM1421 host target gene. C11orf9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C11orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf9 BINDING SITE, designated SEQ ID:14943, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49564] Another function of VGAM1421 is therefore inhibition of Chromosome 11 Open Reading Frame 9 (C11orf9, Accession NM_013279). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf9. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM1421 host target gene. GGA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE, designated SEQ ID:28924, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49565] Another function of VGAM1421 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA1856 (Accession XM_166549) is another VGAM1421 host target gene. KIAA1856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1856 BINDING SITE, designated SEQ ID:44524, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49566] Another function of VGAM1421 is therefore inhibition of KIAA1856 (Accession XM_166549). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1856. MGC10870 (Accession NM_032301) is another VGAM1421 host target gene. MGC10870 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10870 BINDING SITE, designated SEQ ID:26083, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49567] Another function of VGAM1421 is therefore inhibition of MGC10870 (Accession NM_032301). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10870. MGC20460 (Accession NM_053043) is another VGAM1421 host target gene. MGC20460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20460 BINDING SITE, designated SEQ ID:27589, to

the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49568] Another function of VGAM1421 is therefore inhibition of MGC20460 (Accession NM_053043). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20460. Torsin Family 1, Member B (torsin B) (TOR1B, Accession NM_014506) is another VGAM1421 host target gene. TOR1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOR1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOR1B BINDING SITE, designated SEQ ID:15842, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49569] Another function of VGAM1421 is therefore inhibition of Torsin Family 1, Member B (torsin B) (TOR1B, Accession NM_014506). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOR1B. Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM_091895) is an-

other VGAM1421 host target gene. ZNF17 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF17 BINDING SITE, designated SEQ ID:40068, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49570] Another function of VGAM1421 is therefore inhibition of Zinc Finger Protein 17 (HPF3, KOX 10) (ZNF17, Accession XM_091895). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF17. LOC146237 (Accession XM_096954) is another VGAM1421 host target gene. LOC146237 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146237 BINDING SITE, designated SEQ ID:40671, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4132.

[49571] Another function of VGAM1421 is therefore inhibition of LOC146237 (Accession XM_096954). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146237. LOC146733 (Accession XM_097076) is another VGAM1421 host target gene. LOC146733 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146733, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146733 BINDING SITE, designated SEQ ID:40731, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49572] Another function of VGAM1421 is therefore inhibition of LOC146733 (Accession XM_097076). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146733. LOC222183 (Accession XM_168436) is another VGAM1421 host target gene. LOC222183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222183, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222183 BINDING SITE, designated SEQ ID:45185, to the nucleotide sequence of VGAM1421 RNA, herein designated VGAM RNA, also designated SEQ ID:4132.

[49573] Another function of VGAM1421 is therefore inhibition of LOC222183 (Accession XM_168436). Accordingly, utilities of VGAM1421 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222183. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1422 (VGAM1422) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49574] VGAM1422 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1422 was detected is described hereinabove with reference to Figs. 1-8.

[49575] VGAM1422 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Hepatitis GB Virus A.

VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49576] VGAM1422 gene encodes a VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1422 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1422 precursor RNA is designated SEQ ID:1408, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1408 is located at position 1070 relative to the genome of Hepatitis GB Virus A.

[49577] VGAM1422 precursor RNA folds onto itself, forming VGAM1422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49578] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1422 folded precursor RNA into VGAM1422 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1422 RNA is designated SEQ ID:4133, and is provided hereinbelow with reference to the sequence listing part.

[49579] VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1422 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49580] VGAM1422 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1422 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1422 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49581] The complementary binding of VGAM1422 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1422 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1422 host target RNA into VGAM1422 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49582] It is appreciated that VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1422 host target genes. The mRNA of each one of this plurality of VGAM1422 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1422 RNA, herein designated VGAM RNA, and which when bound by VGAM1422 RNA causes inhibition of translation of respective one or more VGAM1422 host target proteins.

[49583] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1422 gene, herein designated VGAM GENE, on one or more VGAM1422 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49584] It is yet further appreciated that a function of VGAM1422 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus A. Specific functions, and accordingly utilities, of VGAM1422 correlate with, and may be deduced from, the identity of the host target genes which VGAM1422 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49585] Nucleotide sequences of the VGAM1422 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1422 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1422 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1422 are further described hereinbelow with reference to Table 1.

[49586] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1422 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1422 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49587] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1422 gene, herein designated VGAM is inhibition of expression of VGAM1422 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1422 correlate with, and may be deduced from, the identity of the target genes which VGAM1422 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49588] CDC-like Kinase 2 (CLK2, Accession NM_001291) is a VGAM1422 host target gene. CLK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLK2 BINDING SITE, designated SEQ ID:6972, to the nucleotide sequence of

VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49589] A function of VGAM1422 is therefore inhibition of CDC-like Kinase 2 (CLK2, Accession NM_001291), a gene which catalyzes the phosphorylation of proteins. Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLK2. The function of CLK2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM356. Dynamin 2 (DNM2, Accession NM_004945) is another VGAM1422 host target gene. DNM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNM2 BINDING SITE, designated SEQ ID:11388, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49590] Another function of VGAM1422 is therefore inhibition of Dynamin 2 (DNM2, Accession NM_004945), a gene which

regulates budding of endocytic vesicles . Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNM2. The function of DNM2 has been established by previous studies. Dynamins (DNMs) are members of a group of GTPases that share high homology in their N-terminal regions. Mammals have at least 3 DNMs: DNM1 (OMIM Ref. No. 602377), DNM2, and DNM3. Diatloff-Zito et al. (1995) had previously isolated a human genomic DNA fragment by its capacity to correct the mitomycin C hypersensitivity of cells from a Fanconi anemia patient belonging to genetic complementation group D (FACD; 227646). Using this fragment, they screened a human fibroblast cDNA library and isolated a cDNA encoding DNM2. The predicted 866-amino acid protein is 73% and 98% identical to DNM1 and rat Dnm2, respectively. It contains the 3 consensus sequence elements characteristic of GTP-binding proteins at its N terminus, a Pleckstrin homology domain, and a basic, proline-rich C-terminal region that contains multiple SRC homology 3 domains. DNM2 contains 9 consensus motifs for CDC2 (OMIM Ref. No. 116940) phosphorylation, indicating a potential role at the G2/mitosis transition. Northern blot analysis de-

tected a 3.6-kb transcript in all tissues examined, with highest expression in heart and skeletal muscle. Sequencing and RT-PCR identified alternative splicing variants of DNM2. The authors suggested that multiple rounds of duplication and divergence occurred within DNM gene evolution. No alterations in DNM2 sequence or mRNA expression were detected in the FACD patient studied. By interspecific backcross analysis, Klocke et al. (1997) found that the mouse Dnm2 gene is closely linked to the Icam1 gene (OMIM Ref. No. 147840) on the proximal portion of chromosome 9, in a region with homologies to human 19p, 8q, and 11q.

[49591] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49592] Diatloff-Zito, C.; Gordon, A. J. E.; Duchaud, E.; Merlin, G. : Isolation of an ubiquitously expressed cDNA encoding human dynamin II, a member of the large GTP-binding protein family. Gene 163: 301-306, 1995. ; and

[49593] Klocke, R.; Augustin, A.; Ronsiek, M.; Stief, A.; van der Putten, H.; Jockusch, H. : Dynamin genes Dnm1 and Dnm2 are located on proximal mouse chromosomes 2 and 9, respectively. Genomic.

[49594] Further studies establishing the function and utilities of DNM2 are found in John Hopkins OMIM database record ID 602378, and in cited publications numbered 5604 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM_030806) is another VGAM1422 host target gene. FLNB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLNB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLNB BINDING SITE, designated SEQ ID:31147, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49595] Another function of VGAM1422 is therefore inhibition of Filamin B, Beta (actin binding protein 278) (FLNB, Accession XM_030806), a gene which Filamin B, beta; binds actin, interacts with cytoplasmic domain of Iba1. Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLNB. The function of FLNB and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM416. Hairless Homolog (mouse) (HR, Accession NM_005144) is another VGAM1422 host target gene. HR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HR BINDING SITE, designated SEQ ID:11619, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49596] Another function of VGAM1422 is therefore inhibition of Hairless Homolog (mouse) (HR, Accession NM_005144). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HR. Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430) is another VGAM1422 host target gene. MN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of MN1 BINDING SITE, designated SEQ ID:8274, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49597] Another function of VGAM1422 is therefore inhibition of Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MN1. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507) is another VGAM1422 host target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, designated SEQ ID:8335, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49598] Another function of VGAM1422 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507), a gene which can me-

mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM212. Retinoic Acid Induced 2 (RAI2, Accession NM_021785) is another VGAM1422 host target gene. RAI2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI2 BINDING SITE, designated SEQ ID:22349, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49599] Another function of VGAM1422 is therefore inhibition of Retinoic Acid Induced 2 (RAI2, Accession NM_021785). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI2. Apg4B (Accession NM_013325) is another VGAM1422 host target gene. Apg4B BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by Apg4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Apg4B BINDING SITE, designated SEQ ID:14975, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49600] Another function of VGAM1422 is therefore inhibition of Apg4B (Accession NM_013325). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Apg4B. D15Wsu75e (Accession XM_039495) is another VGAM1422 host target gene. D15Wsu75e BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by D15Wsu75e, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D15Wsu75e BINDING SITE, designated SEQ ID:33102, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49601] Another function of VGAM1422 is therefore inhibition of

D15Wsu75e (Accession XM_039495). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D15Wsu75e. DLAD (Accession NM_058248) is another VGAM1422 host target gene. DLAD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DLAD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLAD BINDING SITE, designated SEQ ID:27779, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49602] Another function of VGAM1422 is therefore inhibition of DLAD (Accession NM_058248). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLAD. DnaJ (Hsp40) Homolog, Subfamily C, Member 8 (DNAJC8, Accession NM_014280) is another VGAM1422 host target gene. DNAJC8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC8 BINDING SITE, designated SEQ ID:15559, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49603] Another function of VGAM1422 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 8 (DNAJC8, Accession NM_014280). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC8. FLJ14751 (Accession NM_032834) is another VGAM1422 host target gene. FLJ14751 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14751, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14751 BINDING SITE, designated SEQ ID:26612, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49604] Another function of VGAM1422 is therefore inhibition of FLJ14751 (Accession NM_032834). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14751. FLJ23548 (Accession NM_024590) is another VGAM1422 host target gene. FLJ23548 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23548, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23548 BINDING SITE, designated SEQ ID:23827, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49605] Another function of VGAM1422 is therefore inhibition of FLJ23548 (Accession NM_024590). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23548. KIAA1193 (Accession XM_041843) is another VGAM1422 host target gene. KIAA1193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1193 BINDING SITE, designated SEQ ID:33585, to the

nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49606] Another function of VGAM1422 is therefore inhibition of KIAA1193 (Accession XM_041843). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. KIAA1323 (Accession XM_032146) is another VGAM1422 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31565, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49607] Another function of VGAM1422 is therefore inhibition of KIAA1323 (Accession XM_032146). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. KIAA1337 (Accession XM_052561) is another VGAM1422 host target gene. KIAA1337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1337 BINDING SITE, designated SEQ ID:35986, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49608] Another function of VGAM1422 is therefore inhibition of KIAA1337 (Accession XM_052561). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1337. KIAA1705 (Accession XM_051692) is another VGAM1422 host target gene. KIAA1705 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1705 BINDING SITE, designated SEQ ID:35861, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49609] Another function of VGAM1422 is therefore inhibition of KIAA1705 (Accession XM_051692). Accordingly, utilities

of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1705. MGC10715 (Accession NM_024325) is another VGAM1422 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23616, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49610] Another function of VGAM1422 is therefore inhibition of MGC10715 (Accession NM_024325). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. MGC20253 (Accession NM_144583) is another VGAM1422 host target gene. MGC20253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC20253 BINDING SITE, designated SEQ ID:29397, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49611] Another function of VGAM1422 is therefore inhibition of MGC20253 (Accession NM_144583). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20253. Phosphodiesterase 2A, CGMP-stimulated (PDE2A, Accession NM_002599) is another VGAM1422 host target gene. PDE2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE2A BINDING SITE, designated SEQ ID:8463, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49612] Another function of VGAM1422 is therefore inhibition of Phosphodiesterase 2A, CGMP-stimulated (PDE2A, Accession NM_002599). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE2A. LOC123242

(Accession XM_063548) is another VGAM1422 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37242, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49613] Another function of VGAM1422 is therefore inhibition of LOC123242 (Accession XM_063548). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123242. LOC148114 (Accession XM_086050) is another VGAM1422 host target gene. LOC148114 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148114 BINDING SITE, designated SEQ ID:38468, to the nucleotide sequence of VGAM1422 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4133.

[49614] Another function of VGAM1422 is therefore inhibition of LOC148114 (Accession XM_086050). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148114. LOC149086 (Accession XM_097580) is another VGAM1422 host target gene. LOC149086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149086 BINDING SITE, designated SEQ ID:40946, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49615] Another function of VGAM1422 is therefore inhibition of LOC149086 (Accession XM_097580). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149086. LOC151996 (Accession XM_098151) is another VGAM1422 host target gene. LOC151996 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151996, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151996 BINDING SITE, designated SEQ ID:41414, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49616] Another function of VGAM1422 is therefore inhibition of LOC151996 (Accession XM_098151). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151996. LOC253001 (Accession XM_171711) is another VGAM1422 host target gene. LOC253001 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46058, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49617] Another function of VGAM1422 is therefore inhibition of LOC253001 (Accession XM_171711). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC253001. LOC253256 (Accession XM_171506) is another VGAM1422 host target gene. LOC253256 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253256, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253256 BINDING SITE, designated SEQ ID:46048, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49618] Another function of VGAM1422 is therefore inhibition of LOC253256 (Accession XM_171506). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253256. LOC253847 (Accession XM_171145) is another VGAM1422 host target gene. LOC253847 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253847, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253847 BINDING SITE, designated SEQ ID:45941, to

the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49619] Another function of VGAM1422 is therefore inhibition of LOC253847 (Accession XM_171145). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253847. LOC92840 (Accession NM_138393) is another VGAM1422 host target gene. LOC92840 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92840, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92840 BINDING SITE, designated SEQ ID:28761, to the nucleotide sequence of VGAM1422 RNA, herein designated VGAM RNA, also designated SEQ ID:4133.

[49620] Another function of VGAM1422 is therefore inhibition of LOC92840 (Accession NM_138393). Accordingly, utilities of VGAM1422 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92840. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1423 (VGAM1423) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49621] VGAM1423 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1423 was detected is described hereinabove with reference to Figs. 1–8.

[49622] VGAM1423 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Hepatitis GB Virus A. VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49623] VGAM1423 gene encodes a VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1423 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1423 precursor RNA is designated SEQ ID:1409, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1409 is located at position 8372 relative to the genome of Hepatitis GB Virus A.

[49624] VGAM1423 precursor RNA folds onto itself, forming VGAM1423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49625] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1423 folded precursor RNA into VGAM1423 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1423 RNA is designated SEQ ID:4134, and is provided hereinbelow with reference to the sequence listing part.

[49626] VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1423 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1423 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49627] VGAM1423 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1423 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1423 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49628] The complementary binding of VGAM1423 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1423 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1423 host target RNA into VGAM1423 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49629] It is appreciated that VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1423 host target genes. The mRNA of each one of this plurality of VGAM1423 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1423 RNA, herein designated VGAM RNA, and which when bound by VGAM1423 RNA causes inhibition of translation of respective one or more VGAM1423 host target proteins.

[49630] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1423 gene, herein designated VGAM GENE, on one or more VGAM1423 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49631] It is yet further appreciated that a function of VGAM1423 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus A. Specific functions, and accordingly utilities, of VGAM1423 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1423 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49632] Nucleotide sequences of the VGAM1423 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1423 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1423 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1423 are further described hereinbelow with reference to Table 1.

[49633] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1423 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1423 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49634] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1423 gene, herein designated VGAM is inhibition of expression of VGAM1423 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1423 correlate with, and may be deduced from, the identity of the target genes which VGAM1423

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49635] Fibroblast Growth Factor 9 (glia-activating factor) (FGF9, Accession NM_002010) is a VGAM1423 host target gene. FGF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF9 BINDING SITE, designated SEQ ID:7752, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49636] A function of VGAM1423 is therefore inhibition of Fibroblast Growth Factor 9 (glia-activating factor) (FGF9, Accession NM_002010), a gene which Fibroblast growth factor 9 (glia-activating factor); secreted mitogen. Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF9. The function of FGF9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM864. Glypican 4 (GPC4, Accession NM_001448) is another VGAM1423 host target gene.

GPC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC4 BINDING SITE, designated SEQ ID:7176, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49637] Another function of VGAM1423 is therefore inhibition of Glypican 4 (GPC4, Accession NM_001448), a gene which may play a role in growth control and cell division. Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC4. The function of GPC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM538. Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804) is another VGAM1423 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:44842, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49638] Another function of VGAM1423 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Molybdenum Cofactor Synthesis 2 (MOCS2, Accession NM_004531) is another VGAM1423 host target gene. MOCS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOCS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOCS2 BINDING SITE, designated SEQ ID:10874, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49639] Another function of VGAM1423 is therefore inhibition of Molybdenum Cofactor Synthesis 2 (MOCS2, Accession NM_004531). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with MOCS2. Protein Kinase (cAMP-dependent, catalytic) Inhibitor Beta (PKIB, Accession NM_032471) is another VGAM1423 host target gene. PKIB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKIB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIB BINDING SITE, designated SEQ ID:26230, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49640] Another function of VGAM1423 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Beta (PKIB, Accession NM_032471). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIB. Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_007318) is another VGAM1423 host target gene. PSEN1 BINDING SITE1 and PSEN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSEN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PSEN1 BINDING SITE1 and PSEN1 BINDING SITE2, designated SEQ ID:14235 and SEQ ID:5457 respectively, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49641] Another function of VGAM1423 is therefore inhibition of Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_007318). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSEN1. Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349) is another VGAM1423 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3, designated SEQ ID:9368, SEQ ID:22520 and SEQ ID:22767 respectively, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49642] Another function of VGAM1423 is therefore inhibition of

Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM155.FLJ12668 (Accession NM_024997) is another VGAM1423 host target gene. FLJ12668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12668 BINDING SITE, designated SEQ ID:24559, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49643] Another function of VGAM1423 is therefore inhibition of FLJ12668 (Accession NM_024997). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12668. FLJ21916 (Accession NM_023112) is another

VGAM1423 host target gene. FLJ21916 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21916 BINDING SITE, designated SEQ ID:23386, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49644] Another function of VGAM1423 is therefore inhibition of FLJ21916 (Accession NM_023112). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21916. FLJ22127 (Accession NM_022775) is another VGAM1423 host target gene. FLJ22127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22127 BINDING SITE, designated SEQ ID:23043, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49645] Another function of VGAM1423 is therefore inhibition of FLJ22127 (Accession NM_022775). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22127. FLJ22794 (Accession XM_166220) is another VGAM1423 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44033, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49646] Another function of VGAM1423 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. KIAA0493 (Accession XM_034717) is another VGAM1423 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0493 BINDING SITE, designated SEQ ID:32140, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49647] Another function of VGAM1423 is therefore inhibition of KIAA0493 (Accession XM_034717). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. KIAA0515 (Accession XM_033380) is another VGAM1423 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31929, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49648] Another function of VGAM1423 is therefore inhibition of KIAA0515 (Accession XM_033380). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0515. KIAA0795 (Accession NM_025010) is another VGAM1423 host target gene. KIAA0795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0795 BINDING SITE, designated SEQ ID:24587, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49649] Another function of VGAM1423 is therefore inhibition of KIAA0795 (Accession NM_025010). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0795. KIAA0863 (Accession XM_170863) is another VGAM1423 host target gene. KIAA0863 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0863, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0863 BINDING SITE, designated SEQ ID:45635, to the nucleotide sequence of VGAM1423 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4134.

[49650] Another function of VGAM1423 is therefore inhibition of KIAA0863 (Accession XM_170863). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0863. KIAA1068 (Accession NM_015332) is another VGAM1423 host target gene. KIAA1068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1068, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1068 BINDING SITE, designated SEQ ID:17644, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49651] Another function of VGAM1423 is therefore inhibition of KIAA1068 (Accession NM_015332). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1068. KIAA1332 (Accession XM_048774) is another VGAM1423 host target gene. KIAA1332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35259, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49652] Another function of VGAM1423 is therefore inhibition of KIAA1332 (Accession XM_048774). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1545 (Accession XM_027220) is another VGAM1423 host target gene. KIAA1545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1545 BINDING SITE, designated SEQ ID:30442, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49653] Another function of VGAM1423 is therefore inhibition of KIAA1545 (Accession XM_027220). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with KIAA1545. MGC16386 (Accession NM_080668) is another VGAM1423 host target gene. MGC16386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16386 BINDING SITE, designated SEQ ID:27959, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49654] Another function of VGAM1423 is therefore inhibition of MGC16386 (Accession NM_080668). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16386. MGC2560 (Accession NM_031452) is another VGAM1423 host target gene. MGC2560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2560 BINDING SITE, designated SEQ ID:25467, to the nucleotide

sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49655] Another function of VGAM1423 is therefore inhibition of MGC2560 (Accession NM_031452). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2560. LOC127602 (Accession XM_059166) is another VGAM1423 host target gene. LOC127602 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC127602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127602 BINDING SITE, designated SEQ ID:36904, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49656] Another function of VGAM1423 is therefore inhibition of LOC127602 (Accession XM_059166). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127602. LOC149606 (Accession XM_086600) is another VGAM1423 host target gene. LOC149606 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC149606, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149606 BINDING SITE, designated SEQ ID:38786, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49657] Another function of VGAM1423 is therefore inhibition of LOC149606 (Accession XM_086600). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149606. LOC149837 (Accession XM_097747) is another VGAM1423 host target gene. LOC149837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149837 BINDING SITE, designated SEQ ID:41099, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49658] Another function of VGAM1423 is therefore inhibition of LOC149837 (Accession XM_097747). Accordingly, utilities

of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149837. LOC199692 (Accession NM_145295) is another VGAM1423 host target gene. LOC199692 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199692 BINDING SITE, designated SEQ ID:29811, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49659] Another function of VGAM1423 is therefore inhibition of LOC199692 (Accession NM_145295). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199692. LOC202934 (Accession XM_117486) is another VGAM1423 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC202934 BINDING SITE, designated SEQ ID:43458, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49660] Another function of VGAM1423 is therefore inhibition of LOC202934 (Accession XM_117486). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. LOC255465 (Accession XM_173206) is another VGAM1423 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46451, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49661] Another function of VGAM1423 is therefore inhibition of LOC255465 (Accession XM_173206). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. LOC257286 (Accession XM_170549) is another VGAM1423 host target gene. LOC257286 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257286 BINDING SITE, designated SEQ ID:45373, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49662] Another function of VGAM1423 is therefore inhibition of LOC257286 (Accession XM_170549). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257286. LOC90979 (Accession XM_035323) is another VGAM1423 host target gene. LOC90979 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90979, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90979 BINDING SITE, designated SEQ ID:32233, to the nucleotide sequence of VGAM1423 RNA, herein designated VGAM RNA, also designated SEQ ID:4134.

[49663] Another function of VGAM1423 is therefore inhibition of

LOC90979 (Accession XM_035323). Accordingly, utilities of VGAM1423 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90979. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1424 (VGAM1424) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49664] VGAM1424 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1424 was detected is described hereinabove with reference to Figs. 1-8.

[49665] VGAM1424 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49666] VGAM1424 gene encodes a VGAM1424 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1424 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1424 precursor RNA is designated SEQ ID:1410, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1410 is located at position 1464 relative to the genome of Clover Yellow Vein Virus.

- [49667] VGAM1424 precursor RNA folds onto itself, forming VGAM1424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49668] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1424 folded precursor RNA into VGAM1424 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM1424 RNA is designated SEQ ID:4135, and is provided hereinbelow with reference to the sequence listing part.

[49669] VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1424 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49670] VGAM1424 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1424 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1424 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49671] The complementary binding of VGAM1424 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1424 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1424 host target RNA into VGAM1424 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49672] It is appreciated that VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1424 host target genes. The mRNA of each one of this plurality of VGAM1424 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1424 RNA, herein designated VGAM RNA, and which when bound by VGAM1424 RNA causes inhibition of translation of respective one or more VGAM1424 host target proteins.

[49673] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1424 gene, herein designated VGAM GENE, on one or more VGAM1424 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49674] It is yet further appreciated that a function of VGAM1424

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1424 correlate with, and may be deduced from, the identity of the host target genes which VGAM1424 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49675] Nucleotide sequences of the VGAM1424 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1424 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1424 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1424 are further described hereinbelow with reference to Table 1.

[49676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1424 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1424 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49677] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1424 gene, herein designated VGAM is inhibition of expression of VGAM1424 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1424 correlate with, and may be deduced from, the identity of the target genes which VGAM1424 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49678] Syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan) (SDC2, Accession XM_040582) is a VGAM1424 host target gene. SDC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDC2 BINDING SITE, designated SEQ ID:33326, to the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49679] A function of VGAM1424 is therefore inhibition of Syndecan 2 (heparan sulfate proteoglycan 1, cell surface-associated, fibroglycan) (SDC2, Accession XM_040582). Accordingly, utilities of VGAM1424 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with SDC2. KIAA0171 (Accession NM_014666) is another VGAM1424 host target gene. KIAA0171 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0171 BINDING SITE, designated SEQ ID:16121, to the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49680] Another function of VGAM1424 is therefore inhibition of KIAA0171 (Accession NM_014666). Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0171. MOST2 (Accession NM_020250) is another VGAM1424 host target gene. MOST2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOST2 BINDING SITE, designated SEQ ID:21548, to the nucleotide se-

quence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49681] Another function of VGAM1424 is therefore inhibition of MOST2 (Accession NM_020250). Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOST2. Ubiquitin Specific Protease 8 (USP8, Accession NM_005154) is another VGAM1424 host target gene. USP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP8 BINDING SITE, designated SEQ ID:11629, to the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49682] Another function of VGAM1424 is therefore inhibition of Ubiquitin Specific Protease 8 (USP8, Accession NM_005154). Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP8. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM1424 host target gene. ZDHHC2 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18486, to the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49683] Another function of VGAM1424 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC220071 (Accession XM_167848) is another VGAM1424 host target gene. LOC220071 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220071 BINDING SITE, designated SEQ ID:44877, to the nucleotide sequence of VGAM1424 RNA, herein designated VGAM RNA, also designated SEQ ID:4135.

[49684] Another function of VGAM1424 is therefore inhibition of LOC220071 (Accession XM_167848). Accordingly, utilities of VGAM1424 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220071. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1425 (VGAM1425) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49685] VGAM1425 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1425 was detected is described hereinabove with reference to Figs. 1–8.

[49686] VGAM1425 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49687] VGAM1425 gene encodes a VGAM1425 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1425 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1425 precursor RNA is designated SEQ ID:1411, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1411 is located at position 767 relative to the genome of Clover Yellow Vein Virus.

[49688] VGAM1425 precursor RNA folds onto itself, forming VGAM1425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49689] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1425 folded precursor RNA into VGAM1425 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1425 RNA is designated SEQ ID:4136, and is provided hereinbelow with reference to the sequence listing part.

[49690] VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1425 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[49691] VGAM1425 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1425 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1425 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49692] The complementary binding of VGAM1425 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1425 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1425 host target RNA into VGAM1425 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49693] It is appreciated that VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1425 host target genes. The mRNA of each one of this plurality of VGAM1425 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1425 RNA, herein designated VGAM RNA, and which when bound by VGAM1425 RNA causes inhibition of translation of respective one or more VGAM1425 host target proteins.

[49694] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1425 gene, herein designated VGAM GENE, on one or more VGAM1425 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49695] It is yet further appreciated that a function of VGAM1425 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1425 correlate with, and may be deduced from, the identity of the host target genes which VGAM1425 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49696] Nucleotide sequences of the VGAM1425 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1425 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1425 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1425 are further described hereinbelow with reference to Table 1.

[49697] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1425 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1425 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[49698] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1425 gene, herein designated VGAM is inhibition of expression of VGAM1425 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1425 correlate with, and may be deduced from, the identity of the target genes which VGAM1425 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49699] Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is a VGAM1425 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20734, to the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, also designated SEQ ID:4136.

[49700] A function of VGAM1425 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of

VGAM1425 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Vascular Cell Adhesion Molecule 1 (VCAM1, Accession NM_001078) is another VGAM1425 host target gene. VCAM1 BINDING SITE1 and VCAM1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by VCAM1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VCAM1 BINDING SITE1 and VCAM1 BINDING SITE2, designated SEQ ID:6737 and SEQ ID:27983 respectively, to the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, also designated SEQ ID:4136.

[49701] Another function of VGAM1425 is therefore inhibition of Vascular Cell Adhesion Molecule 1 (VCAM1, Accession NM_001078). Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VCAM1. FLJ10852 (Accession NM_019028) is another VGAM1425 host target

gene. FLJ10852 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10852, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10852 BINDING SITE, designated SEQ ID:21117, to the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, also designated SEQ ID:4136.

[49702] Another function of VGAM1425 is therefore inhibition of FLJ10852 (Accession NM_019028). Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10852. MGC4643 (Accession NM_032715) is another VGAM1425 host target gene. MGC4643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4643 BINDING SITE, designated SEQ ID:26438, to the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, also designated SEQ ID:4136.

[49703] Another function of VGAM1425 is therefore inhibition of MGC4643 (Accession NM_032715). Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4643. p25 (Accession NM_007030) is another VGAM1425 host target gene. p25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by p25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of p25 BINDING SITE, designated SEQ ID:13890, to the nucleotide sequence of VGAM1425 RNA, herein designated VGAM RNA, also designated SEQ ID:4136.

[49704] Another function of VGAM1425 is therefore inhibition of p25 (Accession NM_007030). Accordingly, utilities of VGAM1425 include diagnosis, prevention and treatment of diseases and clinical conditions associated with p25. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1426 (VGAM1426) viral gene, which modulates expression of respective host target genes thereof, the function and

utility of which host target genes is known in the art.

[49705] VGAM1426 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1426 was detected is described hereinabove with reference to Figs. 1–8.

[49706] VGAM1426 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49707] VGAM1426 gene encodes a VGAM1426 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1426 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1426 precursor RNA is designated SEQ ID:1412, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1412 is located at position 8366 relative to the genome of Clover Yellow Vein Virus.

[49708] VGAM1426 precursor RNA folds onto itself, forming VGAM1426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49709] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1426 folded precursor RNA into VGAM1426 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1426 RNA is designated SEQ ID:4137, and is provided hereinbelow with reference to the sequence listing part.

[49710] VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1426 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49711] VGAM1426 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1426 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1426 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[49712] The complementary binding of VGAM1426 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1426 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1426 host target RNA into VGAM1426 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49713] It is appreciated that VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1426 host target genes. The mRNA of each one of this plurality of VGAM1426 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1426 RNA, herein designated VGAM RNA, and which when bound by VGAM1426 RNA causes inhibition of translation of respective one or more VGAM1426 host target proteins.

[49714] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1426 gene, herein designated VGAM GENE, on one

or more VGAM1426 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49715] It is yet further appreciated that a function of VGAM1426 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1426 correlate with, and may be deduced from, the identity of the host target genes which VGAM1426 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49716] Nucleotide sequences of the VGAM1426 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1426 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1426 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1426 are further described hereinbelow with reference to Table 1.

[49717] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1426 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1426 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49718] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1426 gene, herein designated VGAM is inhibition of expression of VGAM1426 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1426 correlate with, and may be deduced from, the identity of the target genes which VGAM1426 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49719] Fibroblast Growth Factor Receptor 3 (achondroplasia,

thanatophoric dwarfism) (FGFR3, Accession NM_000142) is a VGAM1426 host target gene. FGFR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGFR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR3 BINDING SITE, designated SEQ ID:5643, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49720] A function of VGAM1426 is therefore inhibition of Fibroblast Growth Factor Receptor 3 (achondroplasia, thanatophoric dwarfism) (FGFR3, Accession NM_000142). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR3. Cyclin M4 (CNNM4, Accession NM_020184) is another VGAM1426 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM4 BINDING SITE, designated SEQ

ID:21422, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49721] Another function of VGAM1426 is therefore inhibition of Cyclin M4 (CNNM4, Accession NM_020184). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM4. DKFZp434N035 (Accession NM_032262) is another VGAM1426 host target gene. DKFZp434N035 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434N035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434N035 BINDING SITE, designated SEQ ID:26006, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49722] Another function of VGAM1426 is therefore inhibition of DKFZp434N035 (Accession NM_032262). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434N035. MGC13138 (Accession NM_033410)

is another VGAM1426 host target gene. MGC13138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13138 BINDING SITE, designated SEQ ID:27232, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49723] Another function of VGAM1426 is therefore inhibition of MGC13138 (Accession NM_033410). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13138. MIDORI (Accession XM_057651) is another VGAM1426 host target gene. MIDORI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIDORI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIDORI BINDING SITE, designated SEQ ID:36530, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49724] Another function of VGAM1426 is therefore inhibition of MIDORI (Accession XM_057651). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIDORI. Serine/threonine Kinase 29 (STK29, Accession XM_113646) is another VGAM1426 host target gene. STK29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK29 BINDING SITE, designated SEQ ID:42319, to the nucleotide sequence of VGAM1426 RNA, herein designated VGAM RNA, also designated SEQ ID:4137.

[49725] Another function of VGAM1426 is therefore inhibition of Serine/threonine Kinase 29 (STK29, Accession XM_113646). Accordingly, utilities of VGAM1426 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK29. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1427

(VGAM1427) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49726] VGAM1427 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1427 was detected is described hereinabove with reference to Figs. 1-8.

[49727] VGAM1427 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49728] VGAM1427 gene encodes a VGAM1427 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1427 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1427 precursor RNA is designated SEQ ID:1413, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1413 is located at position 8119 relative to the genome of Clover Yellow Vein Virus.

[49729] VGAM1427 precursor RNA folds onto itself, forming

VGAM1427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49730] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1427 folded precursor RNA into VGAM1427 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1427 RNA is designated SEQ ID:4138, and is provided hereinbelow with reference to the sequence listing part.

[49731] VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1427 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[49732] VGAM1427 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1427 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1427 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49733] The complementary binding of VGAM1427 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1427 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1427 host target RNA into VGAM1427 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49734] It is appreciated that VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1427 host target genes. The mRNA of each one of this plurality of VGAM1427 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1427 RNA, herein designated VGAM RNA, and which when bound by VGAM1427 RNA causes inhibition of translation of respective one or more VGAM1427 host target proteins.

[49735] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1427 gene, herein designated VGAM GENE, on one or more VGAM1427 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49736] It is yet further appreciated that a function of VGAM1427 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1427 correlate with, and may be deduced from, the identity of the host target genes which VGAM1427 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[49737] Nucleotide sequences of the VGAM1427 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1427 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1427 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1427 are further described hereinbelow with reference to Table 1.

[49738] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1427 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1427 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49739] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1427 gene, herein designated VGAM is inhibition of expression of VGAM1427 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1427 correlate with, and may be deduced from, the identity of the target genes which VGAM1427 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[49740] Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398) is a VGAM1427 host target gene. DLG5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DLG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG5 BINDING SITE, designated SEQ ID:40341, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49741] A function of VGAM1427 is therefore inhibition of Discs, Large (Drosophila) Homolog 5 (DLG5, Accession XM_096398), a gene which may transmit extracellular signals to inhibit cell proliferation. Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG5. The function of DLG5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM444. Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is another VGAM1427 host target gene. FLRT2 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14880, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49742] Another function of VGAM1427 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Nebulin-related Anchoring Protein (Nrap, Accession NM_139235) is another VGAM1427 host target gene. Nrap BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Nrap, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nrap BINDING SITE, designated SEQ ID:29237, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49743] Another function of VGAM1427 is therefore inhibition of Nebulin-related Anchoring Protein (Nrap, Accession NM_139235), a gene which performs an anchoring function to link the terminal actin filaments of myofibrils to protein complexes located beneath the sarcolemma. Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nrap. The function of Nrap and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM649.CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332) is another VGAM1427 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CDC14B BINDING SITE, designated SEQ ID:27173, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49744] Another function of VGAM1427 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. DKFZP434C1715 (Accession XM_098421) is another VGAM1427 host target gene. DKFZP434C1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434C1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434C1715 BINDING SITE, designated SEQ ID:41677, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49745] Another function of VGAM1427 is therefore inhibition of DKFZP434C1715 (Accession XM_098421). Accordingly, utilities of VGAM1427 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP434C1715. KIAA0171 (Accession NM_014666) is another VGAM1427 host target gene. KIAA0171 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0171 BINDING SITE, designated SEQ ID:16123, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49746] Another function of VGAM1427 is therefore inhibition of KIAA0171 (Accession NM_014666). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0171. KIAA0420 (Accession XM_032693) is another VGAM1427 host target gene. KIAA0420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0420 BINDING SITE, designated SEQ ID:31729, to the

nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49747] Another function of VGAM1427 is therefore inhibition of KIAA0420 (Accession XM_032693). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0420. MGC4655 (Accession NM_033309) is another VGAM1427 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655 BINDING SITE, designated SEQ ID:27148, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49748] Another function of VGAM1427 is therefore inhibition of MGC4655 (Accession NM_033309). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. Phosphodiesterase 10A (PDE10A, Accession NM_006661) is another VGAM1427 host target gene. PDE10A BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by PDE10A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE10A BINDING SITE, designated SEQ ID:13465, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49749] Another function of VGAM1427 is therefore inhibition of Phosphodiesterase 10A (PDE10A, Accession NM_006661). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE10A. PPI5PIV (Accession NM_019892) is another VGAM1427 host target gene. PPI5PIV BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPI5PIV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPI5PIV BINDING SITE, designated SEQ ID:21278, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49750] Another function of VGAM1427 is therefore inhibition of PPI5PIV (Accession NM_019892). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPI5PIV. RDH-E2 (Accession NM_138969) is another VGAM1427 host target gene. RDH-E2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDH-E2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDH-E2 BINDING SITE, designated SEQ ID:29080, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49751] Another function of VGAM1427 is therefore inhibition of RDH-E2 (Accession NM_138969). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDH-E2. LOC147632 (Accession NM_138478) is another VGAM1427 host target gene. LOC147632 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147632, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147632 BINDING SITE, designated SEQ ID:28828, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49752] Another function of VGAM1427 is therefore inhibition of LOC147632 (Accession NM_138478). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147632. LOC155061 (Accession XM_088139) is another VGAM1427 host target gene. LOC155061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155061 BINDING SITE, designated SEQ ID:39535, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49753] Another function of VGAM1427 is therefore inhibition of LOC155061 (Accession XM_088139). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC155061. LOC255252 (Accession XM_170779) is another VGAM1427 host target gene. LOC255252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255252 BINDING SITE, designated SEQ ID:45547, to the nucleotide sequence of VGAM1427 RNA, herein designated VGAM RNA, also designated SEQ ID:4138.

[49754] Another function of VGAM1427 is therefore inhibition of LOC255252 (Accession XM_170779). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255252. LOC257354 (Accession XM_170810) is another VGAM1427 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45582, to the nucleotide sequence of VGAM1427 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4138.

[49755] Another function of VGAM1427 is therefore inhibition of LOC257354 (Accession XM_170810). Accordingly, utilities of VGAM1427 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1428 (VGAM1428) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49756] VGAM1428 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1428 was detected is described hereinabove with reference to Figs. 1–8.

[49757] VGAM1428 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49758] VGAM1428 gene encodes a VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1428 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1428 precursor RNA is designated SEQ ID:1414, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1414 is located at position 1573 relative to the genome of Clover Yellow Vein Virus.

- [49759] VGAM1428 precursor RNA folds onto itself, forming VGAM1428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49760] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1428 folded precursor RNA into VGAM1428 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM1428 RNA is designated SEQ ID:4139, and is provided hereinbelow with reference to the sequence listing part.

[49761] VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1428 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49762] VGAM1428 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1428 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1428 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49763] The complementary binding of VGAM1428 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1428 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1428 host target RNA into VGAM1428 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49764] It is appreciated that VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1428 host target genes. The mRNA of

each one of this plurality of VGAM1428 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1428 RNA, herein designated VGAM RNA, and which when bound by VGAM1428 RNA causes inhibition of translation of respective one or more VGAM1428 host target proteins.

[49765] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1428 gene, herein designated VGAM GENE, on one or more VGAM1428 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[49766] It is yet further appreciated that a function of VGAM1428 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1428 correlate with, and may be deduced from, the identity of the host target genes which VGAM1428 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49767] Nucleotide sequences of the VGAM1428 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1428 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1428 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1428 are further described hereinbelow with reference to Table 1.

[49768] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1428 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1428 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49769] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1428 gene, herein designated VGAM is inhibition of expression of VGAM1428 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1428 correlate with, and may be deduced from, the identity of the target genes which VGAM1428 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49770] Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM_054027) is a VGAM1428 host target gene. ANKH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKH BINDING SITE, designated SEQ ID:27637, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49771] A function of VGAM1428 is therefore inhibition of Ankylosis, Progressive Homolog (mouse) (ANKH, Accession NM_054027), a gene which regulates intra- and extracel-

lular levels of inorganic pyrophosphate (ppi), probably functioning as ppi transporter. Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKH. The function of ANKH and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1247. Calcitonin Receptor (CALCR, Accession NM_001742) is another VGAM1428 host target gene. CALCR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALCR BINDING SITE, designated SEQ ID:7476, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49772] Another function of VGAM1428 is therefore inhibition of Calcitonin Receptor (CALCR, Accession NM_001742), a gene which is a receptor for calcitonin, is mediated by g proteins which activate adenylyl cyclase, and thought to couple to the heterotrimeric guanosine triphosphate-bind-

ing protein that is sensitive to cholera toxin. Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALCR. The function of CALCR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM94. Transferrin Receptor (p90, CD71) (TFRC, Accession NM_003234) is another VGAM1428 host target gene. TFRC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFRC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFRC BINDING SITE, designated SEQ ID:9227, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49773] Another function of VGAM1428 is therefore inhibition of Transferrin Receptor (p90, CD71) (TFRC, Accession NM_003234), a gene which is involved in the transferrin cycle and iron adsorption. Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFRC.

The function of TFRC has been established by previous studies. A monoclonal antibody, OKT-9, recognizes an antigen ubiquitously distributed on the cell surface of actively growing human cells. It is a glycoprotein composed of disulfide-linked polypeptide chains, each of 90,000 daltons molecular weight. Immunoprecipitation of the OKT-9 antigen in the presence of labeled transferrin results in specific precipitation of transferrin (Sutherland et al., 1981); thus, the OKT-9 antigen is presumably transferrin receptor. Nikinmaa and Schroder (1987) concluded that p90 and TFRC are the same protein: studies using monoclonal antibodies indicated that exhaustive precipitation of radioactively labeled lysates with one antibody removed all activity of lysates with the other. Peptide maps of antigens recognized with both antibodies showed great similarity and indicated that both antibodies react with the same antigen, the human transferrin receptor, but with different antigenic sites of the molecule. Casey et al. (1988) analyzed the regulation by iron of the TFRC gene by examining mouse cells transformed with chimeric constructs containing the human transferrin receptor gene's promoter and either the structural gene for bacterial chloramphenicol acetyltransferase or the human TFRC

cDNA. They concluded that at least 2 genetic elements, one 5-prime and one 3-prime to the gene, are involved in the regulation of the TFRC gene by iron. Animal model experiments lend further support to the function of TFRC. Levy et al. (1999) disrupted the transferrin receptor gene, which they termed *Trfr*, in mice. Homozygous mutant mice were not viable beyond embryonic day 12.5 and had severe anemia with hydrops as well as diffuse neurologic abnormalities. There was some variation of onset of severe anemia, and in nonanemic embryos without tissue edema and necrosis (E9.5), both stressed erythropoiesis and neurologic abnormalities were apparent. The authors concluded that inadequate iron led to neuronal apoptosis, but that tissues other than erythrocytes and neurons can obtain sufficient iron for growth and development through mechanisms independent of the transferrin cycle. Haploinsufficiency for the transferrin receptor resulted in microcytic, hypochromic erythrocytes; normal hemoglobin and hematocrit values were due to compensatory increase in red cell numbers. Although iron saturation of serum transferrin was indistinguishable from that of wildtype, heterozygotes had significantly less tissue iron.

[49774] It is appreciated that the abovementioned animal model

for TFRC is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[49775] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49776] Nikinmaa, B.; Schroder, J. : Two antigens, the transferrin receptor and p90 assigned to human chromosome 3, are probably the same protein. *Hereditas* 107: 55–58, 1987. ; and

[49777] Levy, J. E.; Jin, O.; Fujiwara, Y.; Kuo, F.; Andrews, N. C. : Transferrin receptor is necessary for development of erythrocytes and the nervous system. *Nature Genet.* 21: 396–399, 1999.

[49778] Further studies establishing the function and utilities of TFRC are found in John Hopkins OMIM database record ID 190010, and in cited publications numbered 10757–10414, 10421–10420, 10422–10424, 55 and 10425–10426 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BM–002 (Accession NM_016617) is another VGAM1428 host target gene. BM–002 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by BM-002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM-002 BINDING SITE, designated SEQ ID:18726, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49779] Another function of VGAM1428 is therefore inhibition of BM-002 (Accession NM_016617). Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM-002. SEC15L (Accession XM_051147) is another VGAM1428 host target gene. SEC15L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC15L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC15L BINDING SITE, designated SEQ ID:35766, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49780] Another function of VGAM1428 is therefore inhibition of SEC15L (Accession XM_051147). Accordingly, utilities of

VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC15L. LOC51667 (Accession NM_016118) is another VGAM1428 host target gene. LOC51667 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51667 BINDING SITE, designated SEQ ID:18199, to the nucleotide sequence of VGAM1428 RNA, herein designated VGAM RNA, also designated SEQ ID:4139.

[49781] Another function of VGAM1428 is therefore inhibition of LOC51667 (Accession NM_016118). Accordingly, utilities of VGAM1428 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51667. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1429 (VGAM1429) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49782] VGAM1429 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1429 was detected is described hereinabove with reference to Figs. 1–8.

[49783] VGAM1429 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49784] VGAM1429 gene encodes a VGAM1429 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1429 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1429 precursor RNA is designated SEQ ID:1415, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1415 is located at position 913 relative to the genome of Clover Yellow Vein Virus.

[49785] VGAM1429 precursor RNA folds onto itself, forming VGAM1429 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49786] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1429 folded precursor RNA into VGAM1429 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM1429 RNA is designated SEQ ID:4140, and is provided hereinbelow with reference to the sequence listing part.

[49787] VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1429 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[49788] VGAM1429 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1429 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1429 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49789] The complementary binding of VGAM1429 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1429 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1429 host target RNA into VGAM1429 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49790] It is appreciated that VGAM1429 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1429 host target genes. The mRNA of each one of this plurality of VGAM1429 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1429 RNA, herein designated VGAM RNA, and which when bound by VGAM1429 RNA causes inhibition of translation of respective one or more VGAM1429 host target proteins.

[49791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1429 gene, herein designated VGAM GENE, on one or more VGAM1429 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49792] It is yet further appreciated that a function of VGAM1429 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGAM1429 correlate with, and may be deduced from, the identity of the host target genes which VGAM1429 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49793] Nucleotide sequences of the VGAM1429 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1429 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1429 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1429 are further
described hereinbelow with reference to Table 1.

[49794] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1429 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1429 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[49795] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1429 gene, herein designated VGAM is
inhibition of expression of VGAM1429 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1429 correlate with, and may be deduced
from, the identity of the target genes which VGAM1429
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[49796] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession
XM_116974) is a VGAM1429 host target gene. AKAP13

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:43173, to the nucleotide sequence of VGAM1429 RNA, herein designated VGAM RNA, also designated SEQ ID:4140.

[49797] A function of VGAM1429 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17. Cytochrome P450, Subfamily XIX (aromatization of androgens) (CYP19, Accession NM_000103) is another VGAM1429 host target gene. CYP19 BINDING SITE1 and CYP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CYP19, corresponding to HOST TARGET

binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP19 BINDING SITE1 and CYP19 BINDING SITE2, designated SEQ ID:5563 and SEQ ID:25273 respectively, to the nucleotide sequence of VGAM1429 RNA, herein designated VGAM RNA, also designated SEQ ID:4140.

[49798] Another function of VGAM1429 is therefore inhibition of Cytochrome P450, Subfamily XIX (aromatization of androgens) (CYP19, Accession NM_000103), a gene which catalyzes the last steps of estrogen biosynthesis. Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP19. The function of CYP19 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM508.KIAA1676 (Accession XM_167612) is another VGAM1429 host target gene. KIAA1676 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of KIAA1676 BINDING SITE, designated SEQ ID:44724, to the nucleotide sequence of VGAM1429 RNA, herein designated VGAM RNA, also designated SEQ ID:4140.

[49799] Another function of VGAM1429 is therefore inhibition of KIAA1676 (Accession XM_167612). Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1676. KIAA1796 (Accession XM_166146) is another VGAM1429 host target gene. KIAA1796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1796 BINDING SITE, designated SEQ ID:43961, to the nucleotide sequence of VGAM1429 RNA, herein designated VGAM RNA, also designated SEQ ID:4140.

[49800] Another function of VGAM1429 is therefore inhibition of KIAA1796 (Accession XM_166146). Accordingly, utilities of VGAM1429 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1796. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1430 (VGAM1430) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49801] VGAM1430 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1430 was detected is described hereinabove with reference to Figs. 1–8.

[49802] VGAM1430 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Clover Yellow Vein Virus. VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49803] VGAM1430 gene encodes a VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1430 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1430 precursor RNA is designated SEQ ID:1416, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1416 is located at position 6030 relative to the genome of Clover Yellow Vein Virus.

[49804] VGAM1430 precursor RNA folds onto itself, forming VGAM1430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49805] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1430 folded precursor RNA into VGAM1430 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM1430 RNA is designated SEQ ID:4141, and is provided hereinbelow with reference to the sequence listing part.

[49806] VGAM1430 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1430 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[49807] VGAM1430 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1430 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1430 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1430 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[49808] The complementary binding of VGAM1430 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1430 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1430 host target RNA into VGAM1430 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49809] It is appreciated that VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1430 host target genes. The mRNA of each one of this plurality of VGAM1430 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1430 RNA, herein designated VGAM RNA, and which when bound by VGAM1430 RNA causes inhibition of translation of respective one or more

VGAM1430 host target proteins.

[49810] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1430 gene, herein designated VGAM GENE, on one or more VGAM1430 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49811] It is yet further appreciated that a function of VGAM1430 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus.

Specific functions, and accordingly utilities, of VGAM1430 correlate with, and may be deduced from, the identity of the host target genes which VGAM1430 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49812] Nucleotide sequences of the VGAM1430 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1430 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1430 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1430 are further described hereinbelow with reference to Table 1.

[49813] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1430 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1430 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49814] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1430 gene, herein designated VGAM is inhibition of expression of VGAM1430 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1430 correlate with, and may be deduced from, the identity of the target genes which VGAM1430 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49815] B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707) is a VGAM1430 host target gene. BCL7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7B BINDING SITE, designated SEQ ID:7436, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49816] A function of VGAM1430 is therefore inhibition of B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707), a gene which is of yet unknown function. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL7B. The function of BCL7B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189.Forkhead Box O1A (rhabdomyosarcoma)

(FOXO1A, Accession NM_002015) is another VGAM1430 host target gene. FOXO1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXO1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXO1A BINDING SITE, designated SEQ ID:7759, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49817] Another function of VGAM1430 is therefore inhibition of Forkhead Box O1A (rhabdomyosarcoma) (FOXO1A, Accession NM_002015), a gene which is a probable transcription factor. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXO1A. The function of FOXO1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM228. Kruppel-like Factor 7 (ubiquitous) (KLF7, Accession NM_003709) is another VGAM1430 host target gene. KLF7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

KLF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLF7 BINDING SITE, designated SEQ ID:9810, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49818] Another function of VGAM1430 is therefore inhibition of Kruppel-like Factor 7 (ubiquitous) (KLF7, Accession NM_003709), a gene which is a transcriptional activator. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLF7. The function of KLF7 has been established by previous studies. Shields et al. (1996) cloned a mouse cDNA, which they named gut-enriched Kruppel-like factor (Gklf), that encodes a member of the Kruppel family of transcription factors. Immunofluorescence revealed that Gklf is localized to the nucleus and is found at highest levels in growth-arrested cells. Shields et al. (1996) found that transfection of Gklf into COS-1 cells causes an inhibition of DNA synthesis. In the mouse, the authors found that Gklf mRNA is most abundant in the colon and is also expressed in the testis, lung, and small intestine. Garrett-Sinha et al. (1996) identified a novel

zinc finger protein whose mRNA is expressed at high levels in the epidermal layer of the skin and in epithelial cells in the tongue, palate, esophagus, stomach, and colon of newborn mice. They named the protein EZF for 'epithelial zinc finger.' By screening a human umbilical vein endothelial cell cDNA library with a cDNA encoding the C-terminal zinc finger region of EKLF (KLF1; 600599), Yet et al. (1998) isolated a cDNA encoding KLF4, which they called EZF. The predicted 470-amino acid KLF4 protein has a proline- and serine-rich N terminus and contains 3 C₂H₂ Kruppel-type zinc fingers at the C terminus. KLF4 also contains a potential nuclear localization signal. The human KLF4 protein shares 91% sequence identity with mouse Ezf. Recombinant KLF4 bound specifically to a probe containing the CACCC core sequence in gel mobility shift assays. In contrast to other members of the EKLF family, which are transcriptional activators, KLF4 functioned as a transcriptional repressor in transient transfection studies. The authors identified both the repression domain and the activation domain within KLF4. Northern blot analysis detected a 3.5-kb KLF4 transcript in RNA from both human umbilical vein endothelial cells and human aortic endothelial cells. By radiation hybrid mapping,

Yet et al. (1998) mapped the human KLF4 gene to 9q31. Garrett-Sinha et al. (1996) mapped the mouse EZF gene to chromosome 4, in close proximity to the thioredoxin gene (OMIM Ref. No. 187700). Animal model experiments lend further support to the function of KLF7. Located at the interface between body and environment, the epidermis must protect the body against toxic agents and dehydration, and protect itself against physical and mechanical stresses. Acquired just before birth and at the last stage of epidermal differentiation, the skin's proteinaceous/lipid barrier creates a surface seal essential for protecting animals against microbial infections and dehydration. Segre et al. (1999) showed that Kruppel-like factor-4 (KLF4), highly expressed in the differentiating layers of epidermis, is both vital to and selective for barrier acquisition. Klf4 -/- mice die shortly after birth due to loss of skin barrier function, as measured by penetration of external dyes and rapid loss of body fluids. The defect was not corrected by grafting of Klf4 -/- skin onto nude mice. Loss of the barrier occurred without morphologic or biochemical alterations to the well-known structural features of epidermis that are essential for mechanical integrity. Instead, late-stage differentiation structures were selectively perturbed,

including the cornified envelope, a likely scaffold for lipid organization. Using suppressive hybridization, Segre et al. (1999) identified 3 transcripts encoding cornified envelope proteins with altered expression in the absence of Klf4. Sprr2a (OMIM Ref. No. 182267) was one, this being the only epidermal gene whose promoter is known to possess a functional Klf4 binding site. These studies provide a new insight into transcriptional governance of barrier function, and pave the way for unraveling the molecular events that orchestrate this essential process

[49819] It is appreciated that the abovementioned animal model for KLF7 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[49820] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49821] Garrett-Sinha, L. A.; Eberspaecher, H.; Seldin, M. F.; de Crombrughe, B. : A gene for a novel zinc-finger protein expressed in differentiated epithelial cells and transiently in certain mesenchymal cells. J. Biol. Chem. 271: 31384-31390, 1996. ; and

[49822] Segre, J. A.; Bauer, C.; Fuchs, E. : Klf4 is a transcription

factor required for establishing the barrier function of the skin. Nature Genet. 22: 356–360, 1999.

[49823] Further studies establishing the function and utilities of KLF7 are found in John Hopkins OMIM database record ID 604865, and in cited publications numbered 2313 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase 4 (MAPK4, Accession NM_002747) is another VGAM1430 host target gene. MAPK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK4 BINDING SITE, designated SEQ ID:8624, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49824] Another function of VGAM1430 is therefore inhibition of Mitogen-activated Protein Kinase 4 (MAPK4, Accession NM_002747), a gene which phosphorylates microtubule-associated protein-2 may promote entry into the cell cycle. Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with MAPK4. The function of MAPK4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM655.FLJ12221 (Accession XM_031342) is another VGAM1430 host target gene. FLJ12221 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12221 BINDING SITE, designated SEQ ID:31345, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49825] Another function of VGAM1430 is therefore inhibition of FLJ12221 (Accession XM_031342). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12221. FLJ13110 (Accession NM_022912) is another VGAM1430 host target gene. FLJ13110 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13110 BINDING SITE, designated SEQ ID:23218, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49826] Another function of VGAM1430 is therefore inhibition of FLJ13110 (Accession NM_022912). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13110. KIAA0350 (Accession XM_028332) is another VGAM1430 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30669, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49827] Another function of VGAM1430 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0350. KIAA1209 (Accession XM_027307) is another VGAM1430 host target gene. KIAA1209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1209 BINDING SITE, designated SEQ ID:30473, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49828] Another function of VGAM1430 is therefore inhibition of KIAA1209 (Accession XM_027307). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1209. Mitochondrial Ribosomal Protein L48 (MRPL48, Accession NM_016055) is another VGAM1430 host target gene. MRPL48 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MRPL48, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL48 BINDING SITE, designated SEQ ID:18128, to the nucleotide sequence of VGAM1430 RNA,

herein designated VGAM RNA, also designated SEQ ID:4141.

[49829] Another function of VGAM1430 is therefore inhibition of Mitochondrial Ribosomal Protein L48 (MRPL48, Accession NM_016055). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL48. LOC204084 (Accession XM_115181) is another VGAM1430 host target gene. LOC204084 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204084 BINDING SITE, designated SEQ ID:43089, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49830] Another function of VGAM1430 is therefore inhibition of LOC204084 (Accession XM_115181). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204084. LOC221964 (Accession XM_168342) is another VGAM1430 host target gene. LOC221964 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221964 BINDING SITE, designated SEQ ID:45110, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49831] Another function of VGAM1430 is therefore inhibition of LOC221964 (Accession XM_168342). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221964. LOC51107 (Accession NM_016022) is another VGAM1430 host target gene. LOC51107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51107 BINDING SITE, designated SEQ ID:18099, to the nucleotide sequence of VGAM1430 RNA, herein designated VGAM RNA, also designated SEQ ID:4141.

[49832] Another function of VGAM1430 is therefore inhibition of

LOC51107 (Accession NM_016022). Accordingly, utilities of VGAM1430 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51107. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1431 (VGAM1431) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49833] VGAM1431 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1431 was detected is described hereinabove with reference to Figs. 1-8.

[49834] VGAM1431 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A.

VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49835] VGAM1431 gene encodes a VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1431 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1431 precursor RNA is designated SEQ ID:1417, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1417 is located at position 4277 relative to the genome of Potato Virus A.

- [49836] VGAM1431 precursor RNA folds onto itself, forming VGAM1431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [49837] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1431 folded precursor RNA into VGAM1431 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide se-

quence of VGAM1431 RNA is designated SEQ ID:4142, and is provided hereinbelow with reference to the sequence listing part.

[49838] VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1431 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49839] VGAM1431 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1431 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1431 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[49840] The complementary binding of VGAM1431 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1431 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1431 host target RNA into VGAM1431 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49841] It is appreciated that VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1431 host target genes. The mRNA of each one of this plurality of VGAM1431 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1431 RNA, herein designated VGAM RNA, and which when bound by VGAM1431 RNA causes inhibition of translation of respective one or more VGAM1431 host target proteins.

[49842] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1431 gene, herein designated VGAM GENE, on one or more VGAM1431 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49843] It is yet further appreciated that a function of VGAM1431

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1431 correlate with, and may be deduced from, the identity of the host target genes which VGAM1431 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49844] Nucleotide sequences of the VGAM1431 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1431 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1431 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1431 are further described hereinbelow with reference to Table 1.

[49845] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1431 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1431 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49846] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1431 gene, herein designated VGAM is inhibition of expression of VGAM1431 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1431 correlate with, and may be deduced from, the identity of the target genes which VGAM1431 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49847] CDC7 Cell Division Cycle 7-like 1 (*S. cerevisiae*) (CDC7L1, Accession NM_003503) is a VGAM1431 host target gene. CDC7L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC7L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC7L1 BINDING SITE, designated SEQ ID:9592, to the nucleotide sequence of VGAM1431 RNA, herein designated VGAM RNA, also designated SEQ ID:4142.

[49848] A function of VGAM1431 is therefore inhibition of CDC7 Cell Division Cycle 7-like 1 (*S. cerevisiae*) (CDC7L1, Accession NM_003503), a gene which may phosphorylate critical substrates that regulate the G1/S phase transition

and/or DNA replication in mammalian cells. Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC7L1. The function of CDC7L1 has been established by previous studies. The Cdc7 protein kinase is essential for the G1/S transition and initiation of DNA replication during the cell division cycle in *S. cerevisiae*. Hsk1 is the *S. pombe* Cdc7 homolog. By searching EST databases for sequences similar to those of Cdc7 and Hsk1, Jiang and Hunter (1997) identified a partial CDC7L1 cDNA. They used the partial cDNA to isolate a full-length cDNA from a HeLa cell library. The predicted 574-amino acid human CDC7L1 protein contains the 11 conserved subdomains found in all protein serine/threonine kinases as well as 3 additional sequences (kinase inserts) between subdomains I and II, VII and VIII, and X and XI. The kinase domains of CDC7L1 and Cdc7 share 44% protein sequence identity. CDC7L1 has a molecular mass of 64 kD by SDS-PAGE. Using immunofluorescence, the authors demonstrated that CDC7L1 was predominantly localized in the nucleus. Immune complexes of epitope-tagged CDC7L1 from mammalian cell lysates phosphorylated histone H1 in vitro. Although the expression levels of CDC7L1 protein

appeared to be constant throughout the cell cycle, the protein kinase activity of CDC7L1 increased during S phase. Jiang and Hunter (1997) suggested that CDC7L1 may phosphorylate critical substrate(s) that regulate the G1/S phase transition and/or DNA replication in mammalian cells. Sato et al. (1997) isolated cDNAs encoding *Xenopus* and human Cdc7 homologs. Northern blot analysis revealed that CDC7L1 is expressed as 2.4-, 3.5-, and 4.4-kb mRNAs. The 3.5-kb transcript was detected in all tissues tested, while the 2.4-kb mRNA was testis-specific. Sato et al. (1997) determined that CDC7L1 phosphorylates the MCM2 (OMIM Ref. No. 116945) and MCM3 (OMIM Ref. No. 602693) proteins in vitro, suggesting that CDC7L1 may regulate DNA replication by modulating MCM functions. Using Northern blot and dot blot analyses, Hess et al. (1998) found that CDC7L1 was expressed in many normal tissues, but was overexpressed in all transformed cell lines tested and in certain tumor types.

[49849] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[49850] Jiang, W.; Hunter, T. : Identification and characterization of a human protein kinase related to budding yeast

Cdc7p. Proc. Nat. Acad. Sci. 94: 14320–14325, 1997. ;
and

[49851] Hess, G. F.; Drong, R. F.; Weiland, K. L.; Slightom, J. L.;
Sclafani, R. A.; Hollingsworth, R. E. : A human homolog of
the yeast CDC7 gene is overexpressed in some tumors
and transformed.

[49852] Further studies establishing the function and utilities of
CDC7L1 are found in John Hopkins OMIM database record
ID 603311, and in cited publications numbered
2447–2448, 528 and 5832 listed in the bibliography sec-
tion hereinbelow, which are also hereby incorporated by
reference. Chromosome 20 Open Reading Frame 30
(C20orf30, Accession NM_014145) is another VGAM1431
host target gene. C20orf30 BINDING SITE is HOST TARGET
binding site found in the 3` untranslated region of mRNA
encoded by C20orf30, corresponding to a HOST TARGET
binding site such as BINDING SITE I, BINDING SITE II or
BINDING SITE III. Table 2 illustrates the complementarity
of the nucleotide sequences of C20orf30 BINDING SITE,
designated SEQ ID:15429, to the nucleotide sequence of
VGAM1431 RNA, herein designated VGAM RNA, also des-
ignated SEQ ID:4142.

[49853] Another function of VGAM1431 is therefore inhibition of

Chromosome 20 Open Reading Frame 30 (C20orf30, Accession NM_014145). Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf30.

MGC12335 (Accession NM_032744) is another VGAM1431 host target gene. MGC12335 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12335 BINDING SITE, designated SEQ ID:26475, to the nucleotide sequence of VGAM1431 RNA, herein designated VGAM RNA, also designated SEQ ID:4142.

[49854] Another function of VGAM1431 is therefore inhibition of MGC12335 (Accession NM_032744). Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12335. LOC92305 (Accession NM_138385) is another VGAM1431 host target gene. LOC92305 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92305, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92305 BINDING SITE, designated SEQ ID:28760, to the nucleotide sequence of VGAM1431 RNA, herein designated VGAM RNA, also designated SEQ ID:4142.

[49855] Another function of VGAM1431 is therefore inhibition of LOC92305 (Accession NM_138385). Accordingly, utilities of VGAM1431 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92305. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1432 (VGAM1432) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49856] VGAM1432 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1432 was detected is described hereinabove with reference to Figs. 1–8.

[49857] VGAM1432 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A. VGAM1432 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[49858] VGAM1432 gene encodes a VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1432 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1432 precursor RNA is designated SEQ ID:1418, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1418 is located at position 462 relative to the genome of Potato Virus A.

[49859] VGAM1432 precursor RNA folds onto itself, forming VGAM1432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49860] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1432 folded precursor RNA into VGAM1432

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1432 RNA is designated SEQ ID:4143, and is provided hereinbelow with reference to the sequence listing part.

[49861] VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1432 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49862] VGAM1432 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1432 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1432 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49863] The complementary binding of VGAM1432 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1432 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1432 host target RNA into VGAM1432 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[49864] It is appreciated that VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1432 host target genes. The mRNA of each one of this plurality of VGAM1432 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1432 RNA, herein designated VGAM RNA, and which when bound by VGAM1432 RNA causes inhibition of translation of respective one or more VGAM1432 host target proteins.

[49865] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1432 gene, herein designated VGAM GENE, on one or more VGAM1432 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49866] It is yet further appreciated that a function of VGAM1432 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1432 correlate with, and may be deduced from, the identity of the host target genes which VGAM1432 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49867] Nucleotide sequences of the VGAM1432 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1432 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1432 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1432 are further described hereinbelow with reference to Table 1.

[49868] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1432 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1432 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49869] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1432 gene, herein designated VGAM is inhibition of expression of VGAM1432 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1432 correlate with, and may be deduced from, the identity of the target genes which VGAM1432 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49870] Cell Division Cycle 42 (GTP binding protein, 25kDa) (CDC42, Accession NM_001791) is a VGAM1432 host target gene. CDC42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDC42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42 BINDING SITE, designated SEQ ID:7541, to the nucleotide sequence of VGAM1432 RNA,

herein designated VGAM RNA, also designated SEQ ID:4143.

[49871] A function of VGAM1432 is therefore inhibition of Cell Division Cycle 42 (GTP binding protein, 25kDa) (CDC42, Accession NM_001791). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC42. Inositol Polyphosphate-5-phosphatase, 40kDa (INPP5A, Accession NM_005539) is another VGAM1432 host target gene. INPP5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5A BINDING SITE, designated SEQ ID:12065, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49872] Another function of VGAM1432 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 40kDa (INPP5A, Accession NM_005539), a gene which hydrolyzes the calcium-mobilizing second messenger $\text{ins}(1,4,5)\text{p3}$. Accordingly, utilities of VGAM1432 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with INPP5A. The function of INPP5A and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM1305. Kinesin Family Member 5C (KIF5C, Accession NM_004522) is another VGAM1432 host target gene. KIF5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF5C BINDING SITE, designated SEQ ID:10860, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49873] Another function of VGAM1432 is therefore inhibition of Kinesin Family Member 5C (KIF5C, Accession NM_004522). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF5C. Muscleblind-like (Drosophila) (MBNL, Accession NM_021038) is another VGAM1432 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBNL BINDING SITE, designated SEQ ID:22025, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49874] Another function of VGAM1432 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95.Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268) is another VGAM1432 host target gene. REQ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by REQ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of REQ BINDING SITE, designated SEQ ID:12949, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49875] Another function of VGAM1432 is therefore inhibition of Requiem, Apoptosis Response Zinc Finger Gene (REQ, Accession NM_006268), a gene which is a putative zinc finger that is required for apoptosis in murine myeloid cell lines. Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REQ. The function of REQ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. SH3-domain Binding Protein 4 (SH3BP4, Accession NM_014521) is another VGAM1432 host target gene. SH3BP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP4 BINDING SITE, designated SEQ ID:15851, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM

RNA, also designated SEQ ID:4143.

[49876] Another function of VGAM1432 is therefore inhibition of SH3-domain Binding Protein 4 (SH3BP4, Accession NM_014521), a gene which is of unknown function, contains SH3-domain binding protein 4; similar to the EH-binding protein. Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP4. The function of SH3BP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Transducin (beta)-like 1X-linked (TBL1X, Accession NM_005647) is another VGAM1432 host target gene. TBL1X BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBL1X, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL1X BINDING SITE, designated SEQ ID:12179, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49877] Another function of VGAM1432 is therefore inhibition of

Transducin (beta)-like 1X-linked (TBL1X, Accession NM_005647), a gene which activates latent HDAC3 activity. Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL1X. The function of TBL1X and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1151. Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063) is another VGAM1432 host target gene. EML4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EML4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EML4 BINDING SITE, designated SEQ ID:21142, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49878] Another function of VGAM1432 is therefore inhibition of Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EML4.

FLJ00007 (Accession XM_048928) is another VGAM1432 host target gene. FLJ00007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00007 BINDING SITE, designated SEQ ID:35307, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49879] Another function of VGAM1432 is therefore inhibition of FLJ00007 (Accession XM_048928). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00007. FLJ21302 (Accession NM_022901) is another VGAM1432 host target gene. FLJ21302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21302 BINDING SITE, designated SEQ ID:23182, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM

RNA, also designated SEQ ID:4143.

[49880] Another function of VGAM1432 is therefore inhibition of FLJ21302 (Accession NM_022901). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21302. FLJ22596 (Accession NM_025086) is another VGAM1432 host target gene. FLJ22596 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22596 BINDING SITE, designated SEQ ID:24702, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49881] Another function of VGAM1432 is therefore inhibition of FLJ22596 (Accession NM_025086). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22596. FLJ22625 (Accession NM_024715) is another VGAM1432 host target gene. FLJ22625 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22625, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22625 BINDING SITE, designated SEQ ID:24041, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49882] Another function of VGAM1432 is therefore inhibition of FLJ22625 (Accession NM_024715). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22625. FLJ23462 (Accession NM_024843) is another VGAM1432 host target gene. FLJ23462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23462 BINDING SITE, designated SEQ ID:24261, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49883] Another function of VGAM1432 is therefore inhibition of FLJ23462 (Accession NM_024843). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ23462. KIAA1879 (Accession XM_056635) is another VGAM1432 host target gene. KIAA1879 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1879 BINDING SITE, designated SEQ ID:36411, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49884] Another function of VGAM1432 is therefore inhibition of KIAA1879 (Accession XM_056635). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1879. KOC1 (Accession XM_165847) is another VGAM1432 host target gene. KOC1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KOC1 BINDING SITE, designated SEQ ID:43778, to the nucleotide sequence of

VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49885] Another function of VGAM1432 is therefore inhibition of KOC1 (Accession XM_165847). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KOC1. MYLE (Accession NM_014015) is another VGAM1432 host target gene. MYLE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYLE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYLE BINDING SITE, designated SEQ ID:15234, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49886] Another function of VGAM1432 is therefore inhibition of MYLE (Accession NM_014015). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYLE. RAB40B, Member RAS Oncogene Family (RAB40B, Accession NM_006822) is another VGAM1432 host target gene. RAB40B BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by RAB40B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40B BINDING SITE, designated SEQ ID:13694, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49887] Another function of VGAM1432 is therefore inhibition of RAB40B, Member RAS Oncogene Family (RAB40B, Accession NM_006822). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40B. YKT6 (Accession NM_006555) is another VGAM1432 host target gene. YKT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YKT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YKT6 BINDING SITE, designated SEQ ID:13319, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49888] Another function of VGAM1432 is therefore inhibition of

YKT6 (Accession NM_006555). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YKT6. LOC122970 (Accession XM_058672) is another VGAM1432 host target gene. LOC122970 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122970 BINDING SITE, designated SEQ ID:36714, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49889] Another function of VGAM1432 is therefore inhibition of LOC122970 (Accession XM_058672). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122970. LOC149992 (Accession XM_086756) is another VGAM1432 host target gene. LOC149992 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149992 BINDING SITE, designated SEQ ID:38842, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49890] Another function of VGAM1432 is therefore inhibition of LOC149992 (Accession XM_086756). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149992. LOC153339 (Accession XM_098362) is another VGAM1432 host target gene. LOC153339 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153339 BINDING SITE, designated SEQ ID:41613, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49891] Another function of VGAM1432 is therefore inhibition of LOC153339 (Accession XM_098362). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153339. LOC153910 (Accession XM_087801) is an-

other VGAM1432 host target gene. LOC153910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153910 BINDING SITE, designated SEQ ID:39438, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49892] Another function of VGAM1432 is therefore inhibition of LOC153910 (Accession XM_087801). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153910. LOC196955 (Accession XM_085210) is another VGAM1432 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37932, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49893] Another function of VGAM1432 is therefore inhibition of LOC196955 (Accession XM_085210). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC202347 (Accession XM_117390) is another VGAM1432 host target gene. LOC202347 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202347 BINDING SITE, designated SEQ ID:43430, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49894] Another function of VGAM1432 is therefore inhibition of LOC202347 (Accession XM_117390). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202347. LOC219401 (Accession XM_166706) is another VGAM1432 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44590, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49895] Another function of VGAM1432 is therefore inhibition of LOC219401 (Accession XM_166706). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC255012 (Accession XM_171369) is another VGAM1432 host target gene. LOC255012 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255012, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255012 BINDING SITE, designated SEQ ID:46043, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49896] Another function of VGAM1432 is therefore inhibition of LOC255012 (Accession XM_171369). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255012. LOC255096 (Accession XM_174913) is another VGAM1432 host target gene. LOC255096 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255096 BINDING SITE, designated SEQ ID:46606, to the nucleotide sequence of VGAM1432 RNA, herein designated VGAM RNA, also designated SEQ ID:4143.

[49897] Another function of VGAM1432 is therefore inhibition of LOC255096 (Accession XM_174913). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255096. LOC90309 (Accession XM_030830) is another VGAM1432 host target gene. LOC90309 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90309, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90309 BINDING SITE, designated SEQ ID:31150, to the nucleotide sequence of VGAM1432 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4143.

[49898] Another function of VGAM1432 is therefore inhibition of LOC90309 (Accession XM_030830). Accordingly, utilities of VGAM1432 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90309. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1433 (VGAM1433) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49899] VGAM1433 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1433 was detected is described hereinabove with reference to Figs. 1–8.

[49900] VGAM1433 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A. VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49901] VGAM1433 gene encodes a VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1433 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1433 precursor RNA is designated SEQ ID:1419, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1419 is located at position 3612 relative to the genome of Potato Virus A.

[49902] VGAM1433 precursor RNA folds onto itself, forming VGAM1433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49903] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1433 folded precursor RNA into VGAM1433 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1433 RNA is designated SEQ ID:4144, and is provided hereinbelow with reference to the sequence listing part.

[49904] VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1433 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49905] VGAM1433 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1433 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1433 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49906] The complementary binding of VGAM1433 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1433 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1433 host target RNA into VGAM1433 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49907] It is appreciated that VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1433 host target genes. The mRNA of

each one of this plurality of VGAM1433 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1433 RNA, herein designated VGAM RNA, and which when bound by VGAM1433 RNA causes inhibition of translation of respective one or more VGAM1433 host target proteins.

[49908] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1433 gene, herein designated VGAM GENE, on one or more VGAM1433 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[49909] It is yet further appreciated that a function of VGAM1433 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1433 correlate with, and may be deduced from, the identity of the host target genes which VGAM1433 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49910] Nucleotide sequences of the VGAM1433 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1433 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1433 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1433 are further described hereinbelow with reference to Table 1.

[49911] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1433 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1433 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49912] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1433 gene, herein designated VGAM is inhibition of expression of VGAM1433 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1433 correlate with, and may be deduced from, the identity of the target genes which VGAM1433 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49913] B-cell CLL/lymphoma 2 (BCL2, Accession NM_000633) is a VGAM1433 host target gene. BCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2 BINDING SITE, designated SEQ ID:6264, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49914] A function of VGAM1433 is therefore inhibition of B-cell CLL/lymphoma 2 (BCL2, Accession NM_000633). Accordingly, utilities of VGAM1433 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with BCL2. Norrie Disease (pseudoglioma) (NDP, Accession NM_000266) is another VGAM1433 host target gene. NDP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDP BINDING SITE, designated SEQ ID:5806, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49915] Another function of VGAM1433 is therefore inhibition of Norrie Disease (pseudoglioma) (NDP, Accession NM_000266), a gene which may be involved in a pathway that regulates neural cell differentiation and proliferation. Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDP. The function of NDP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM113. Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449) is another VGAM1433 host target gene.

RFX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6050, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49916] Another function of VGAM1433 is therefore inhibition of Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449), a gene which activates transcription from class ii mhc promoters. Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55.FLJ21148 (Accession NM_024860) is another VGAM1433 host target gene. FLJ21148 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21148, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ21148 BINDING SITE, designated SEQ ID:24293, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49917] Another function of VGAM1433 is therefore inhibition of FLJ21148 (Accession NM_024860). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21148. KIAA1671 (Accession XM_037809) is another VGAM1433 host target gene. KIAA1671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1671 BINDING SITE, designated SEQ ID:32691, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49918] Another function of VGAM1433 is therefore inhibition of KIAA1671 (Accession XM_037809). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1671. KIAA1678 (Accession XM_051221) is another

VGAM1433 host target gene. KIAA1678 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1678 BINDING SITE, designated SEQ ID:35789, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49919] Another function of VGAM1433 is therefore inhibition of KIAA1678 (Accession XM_051221). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1678. MGC2562 (Accession NM_032374) is another VGAM1433 host target gene. MGC2562 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2562 BINDING SITE, designated SEQ ID:26165, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49920] Another function of VGAM1433 is therefore inhibition of MGC2562 (Accession NM_032374). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2562. NYD-SP25 (Accession NM_033516) is another VGAM1433 host target gene. NYD-SP25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NYD-SP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP25 BINDING SITE, designated SEQ ID:27293, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49921] Another function of VGAM1433 is therefore inhibition of NYD-SP25 (Accession NM_033516). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP25. Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM_015550) is another VGAM1433 host target gene. OSBPL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL3 BINDING SITE, designated SEQ ID:17814, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49922] Another function of VGAM1433 is therefore inhibition of Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM_015550). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL3. PRO2958 (Accession NM_018546) is another VGAM1433 host target gene. PRO2958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2958 BINDING SITE, designated SEQ ID:20627, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49923] Another function of VGAM1433 is therefore inhibition of PRO2958 (Accession NM_018546). Accordingly, utilities of

VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2958. Retinoic Acid Induced 17 (RAI17, Accession XM_166091) is another VGAM1433 host target gene. RAI17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAI17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI17 BINDING SITE, designated SEQ ID:43858, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49924] Another function of VGAM1433 is therefore inhibition of Retinoic Acid Induced 17 (RAI17, Accession XM_166091). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI17. LOC145508 (Accession XM_085158) is another VGAM1433 host target gene. LOC145508 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC145508 BINDING SITE, designated SEQ ID:37888, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49925] Another function of VGAM1433 is therefore inhibition of LOC145508 (Accession XM_085158). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145508. LOC149566 (Accession XM_097670) is another VGAM1433 host target gene. LOC149566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149566 BINDING SITE, designated SEQ ID:41017, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49926] Another function of VGAM1433 is therefore inhibition of LOC149566 (Accession XM_097670). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149566. LOC253639 (Accession XM_171060) is an-

other VGAM1433 host target gene. LOC253639 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253639 BINDING SITE, designated SEQ ID:45856, to the nucleotide sequence of VGAM1433 RNA, herein designated VGAM RNA, also designated SEQ ID:4144.

[49927] Another function of VGAM1433 is therefore inhibition of LOC253639 (Accession XM_171060). Accordingly, utilities of VGAM1433 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253639. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1434 (VGAM1434) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49928] VGAM1434 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1434 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[49929] VGAM1434 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A.

VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49930] VGAM1434 gene encodes a VGAM1434 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1434 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1434 precursor RNA is designated SEQ ID:1420, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1420 is located at position 3882 relative to the genome of Potato Virus A.

[49931] VGAM1434 precursor RNA folds onto itself, forming VGAM1434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49932] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1434 folded precursor RNA into VGAM1434 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1434 RNA is designated SEQ ID:4145, and is provided hereinbelow with reference to the sequence listing part.

[49933] VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1434 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49934] VGAM1434 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1434 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1434 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1434 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49935] The complementary binding of VGAM1434 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1434 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1434 host target RNA into VGAM1434 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49936] It is appreciated that VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1434 host target genes. The mRNA of each one of this plurality of VGAM1434 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1434 RNA, herein designated VGAM RNA, and which when bound by VGAM1434 RNA causes inhibition of translation of respective one or more VGAM1434 host target proteins.

[49937] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1434 gene, herein designated VGAM GENE, on one or more VGAM1434 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49938] It is yet further appreciated that a function of VGAM1434 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1434 correlate with, and may be deduced from, the identity of the host target genes which VGAM1434 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49939] Nucleotide sequences of the VGAM1434 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1434 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1434 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1434 are further described hereinbelow with reference to Table 1.

[49940] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1434 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1434 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49941] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1434 gene, herein designated VGAM is inhibition of expression of VGAM1434 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1434 correlate with, and may be deduced from, the identity of the target genes which VGAM1434 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49942] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM_013252) is a VGAM1434 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLECSF5,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14916, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49943] A function of VGAM1434 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM_013252). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Usher Syndrome 3A (USH3A, Accession NM_052995) is another VGAM1434 host target gene. USH3A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by USH3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USH3A BINDING SITE, designated SEQ ID:27563, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49944] Another function of VGAM1434 is therefore inhibition of Usher Syndrome 3A (USH3A, Accession NM_052995). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USH3A. FLJ10846 (Accession NM_018241) is another VGAM1434 host target gene. FLJ10846 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10846 BINDING SITE, designated SEQ ID:20197, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49945] Another function of VGAM1434 is therefore inhibition of FLJ10846 (Accession NM_018241). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10846. Mitochondrial Ribosomal Protein S35 (MRPS35, Accession NM_021821) is another VGAM1434 host target gene. MRPS35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS35, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS35 BINDING SITE, designated SEQ ID:22400, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49946] Another function of VGAM1434 is therefore inhibition of Mitochondrial Ribosomal Protein S35 (MRPS35, Accession NM_021821). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS35. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263) is another VGAM1434 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10459, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49947] Another function of VGAM1434 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. LOC90120 (Accession XM_029168) is another VGAM1434 host target gene. LOC90120 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90120, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90120 BINDING SITE, designated SEQ ID:30851, to the nucleotide sequence of VGAM1434 RNA, herein designated VGAM RNA, also designated SEQ ID:4145.

[49948] Another function of VGAM1434 is therefore inhibition of LOC90120 (Accession XM_029168). Accordingly, utilities of VGAM1434 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90120. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1435 (VGAM1435) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49949] VGAM1435 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1435 was detected is described hereinabove with reference to Figs. 1–8.

[49950] VGAM1435 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A. VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49951] VGAM1435 gene encodes a VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1435 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1435 precursor RNA is designated SEQ ID:1421, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1421 is located at position 7490 relative to the

genome of Potato Virus A.

[49952] VGAM1435 precursor RNA folds onto itself, forming VGAM1435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49953] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1435 folded precursor RNA into VGAM1435 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1435 RNA is designated SEQ ID:4146, and is provided hereinbelow with reference to the sequence listing part.

[49954] VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1435 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49955] VGAM1435 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1435 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1435 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49956] The complementary binding of VGAM1435 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1435 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1435 host target RNA into VGAM1435 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[49957] It is appreciated that VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1435 host target genes. The mRNA of each one of this plurality of VGAM1435 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1435 RNA, herein designated VGAM RNA, and which when bound by VGAM1435 RNA causes inhibition of translation of respective one or more VGAM1435 host target proteins.

[49958] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1435 gene, herein designated VGAM GENE, on one or more VGAM1435 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49959] It is yet further appreciated that a function of VGAM1435 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1435 corre-

late with, and may be deduced from, the identity of the host target genes which VGAM1435 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49960] Nucleotide sequences of the VGAM1435 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1435 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1435 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1435 are further described hereinbelow with reference to Table 1.

[49961] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1435 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1435 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49962] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1435 gene, herein designated VGAM is inhibition of expression of VGAM1435 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1435 correlate with, and may be deduced

from, the identity of the target genes which VGAM1435 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49963] DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366) is a VGAM1435 host target gene. DFFB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DFFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DFFB BINDING SITE, designated SEQ ID:42237, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49964] A function of VGAM1435 is therefore inhibition of DNA Fragmentation Factor, 40kDa, Beta Polypeptide (caspase-activated DNase) (DFFB, Accession XM_113366), a gene which induces DNA fragmentation and chromatin condensation during apoptosis. Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DFFB. The function of DFFB and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM74. Endothelin 3 (EDN3, Accession NM_000114) is another VGAM1435 host target gene. EDN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EDN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EDN3 BINDING SITE, designated SEQ ID:5581, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49965] Another function of VGAM1435 is therefore inhibition of Endothelin 3 (EDN3, Accession NM_000114). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EDN3. Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM_001732) is another VGAM1435 host target gene. BTN1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN1A1 BINDING SITE,

designated SEQ ID:7469, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49966] Another function of VGAM1435 is therefore inhibition of Butyrophilin, Subfamily 1, Member A1 (BTN1A1, Accession NM_001732). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN1A1. KIAA0121 (Accession XM_052386) is another VGAM1435 host target gene. KIAA0121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0121 BINDING SITE, designated SEQ ID:35965, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49967] Another function of VGAM1435 is therefore inhibition of KIAA0121 (Accession XM_052386). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. MGC3265 (Accession NM_024028) is another

VGAM1435 host target gene. MGC3265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3265 BINDING SITE, designated SEQ ID:23457, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49968] Another function of VGAM1435 is therefore inhibition of MGC3265 (Accession NM_024028). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3265. Ubinuclein 1 (UBN1, Accession NM_016936) is another VGAM1435 host target gene. UBN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBN1 BINDING SITE, designated SEQ ID:18852, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49969] Another function of VGAM1435 is therefore inhibition of Ubinuclein 1 (UBN1, Accession NM_016936). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBN1. LOC146723 (Accession XM_085565) is another VGAM1435 host target gene. LOC146723 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146723, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146723 BINDING SITE, designated SEQ ID:38227, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49970] Another function of VGAM1435 is therefore inhibition of LOC146723 (Accession XM_085565). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146723. LOC158158 (Accession XM_088494) is another VGAM1435 host target gene. LOC158158 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158158, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158158 BINDING SITE, designated SEQ ID:39732, to the nucleotide sequence of VGAM1435 RNA, herein designated VGAM RNA, also designated SEQ ID:4146.

[49971] Another function of VGAM1435 is therefore inhibition of LOC158158 (Accession XM_088494). Accordingly, utilities of VGAM1435 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158158. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1436 (VGAM1436) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49972] VGAM1436 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1436 was detected is described hereinabove with reference to Figs. 1-8.

[49973] VGAM1436 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A. VGAM1436 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[49974] VGAM1436 gene encodes a VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1436 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1436 precursor RNA is designated SEQ ID:1422, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1422 is located at position 6614 relative to the genome of Potato Virus A.

[49975] VGAM1436 precursor RNA folds onto itself, forming VGAM1436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49976] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1436 folded precursor RNA into VGAM1436

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM1436 RNA is designated SEQ ID:4147, and is provided hereinbelow with reference to the sequence listing part.

[49977] VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1436 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49978] VGAM1436 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1436 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1436 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49979] The complementary binding of VGAM1436 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1436 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1436 host target RNA into VGAM1436 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[49980] It is appreciated that VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1436 host target genes. The mRNA of each one of this plurality of VGAM1436 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1436 RNA, herein designated VGAM RNA, and which when bound by VGAM1436 RNA causes inhibition of translation of respective one or more VGAM1436 host target proteins.

[49981] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1436 gene, herein designated VGAM GENE, on one or more VGAM1436 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[49982] It is yet further appreciated that a function of VGAM1436 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1436 correlate with, and may be deduced from, the identity of the host target genes which VGAM1436 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[49983] Nucleotide sequences of the VGAM1436 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1436 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1436 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1436 are further described hereinbelow with reference to Table 1.

[49984] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1436 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1436 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[49985] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1436 gene, herein designated VGAM is inhibition of expression of VGAM1436 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1436 correlate with, and may be deduced from, the identity of the target genes which VGAM1436 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[49986] Human Immunodeficiency Virus Type I Enhancer Binding Protein 2 (HIVEP2, Accession NM_006734) is a VGAM1436 host target gene. HIVEP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIVEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIVEP2 BINDING SITE, designated SEQ ID:13586, to the nucleotide sequence of

VGAM1436 RNA, herein designated VGAM RNA, also designated SEQ ID:4147.

[49987] A function of VGAM1436 is therefore inhibition of Human Immunodeficiency Virus Type I Enhancer Binding Protein 2 (HIVEP2, Accession NM_006734). Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIVEP2. Synaptotagmin I (SYT1, Accession NM_005639) is another VGAM1436 host target gene. SYT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT1 BINDING SITE, designated SEQ ID:12167, to the nucleotide sequence of VGAM1436 RNA, herein designated VGAM RNA, also designated SEQ ID:4147.

[49988] Another function of VGAM1436 is therefore inhibition of Synaptotagmin I (SYT1, Accession NM_005639), a gene which may have a regulatory role in the membrane interactions during trafficking of synaptic vesicles at the active zone of the synapse. Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with SYT1. The function of SYT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM739. Zinc Finger Protein 278 (ZNF278, Accession NM_014323) is another VGAM1436 host target gene. ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ZNF278, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF278 BINDING SITE1 through ZNF278 BINDING SITE3, designated SEQ ID:15626, SEQ ID:25775 and SEQ ID:25785 respectively, to the nucleotide sequence of VGAM1436 RNA, herein designated VGAM RNA, also designated SEQ ID:4147.

[49989] Another function of VGAM1436 is therefore inhibition of Zinc Finger Protein 278 (ZNF278, Accession NM_014323), a gene which represses basal transcription as well as RNF4-mediated activation. Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF278. The function of ZNF278 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM414. Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202) is another VGAM1436 host target gene. SS18L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SS18L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS18L1 BINDING SITE, designated SEQ ID:32556, to the nucleotide sequence of VGAM1436 RNA, herein designated VGAM RNA, also designated SEQ ID:4147.

[49990] Another function of VGAM1436 is therefore inhibition of Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202). Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18L1. LOC145815 (Accession XM_096874) is another VGAM1436 host target gene. LOC145815 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145815, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145815 BINDING SITE, designated SEQ ID:40602, to the nucleotide sequence of VGAM1436 RNA, herein designated VGAM RNA, also designated SEQ ID:4147.

[49991] Another function of VGAM1436 is therefore inhibition of LOC145815 (Accession XM_096874). Accordingly, utilities of VGAM1436 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145815. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1437 (VGAM1437) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[49992] VGAM1437 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1437 was detected is described hereinabove with reference to Figs. 1-8.

[49993] VGAM1437 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Potato Virus A.

VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[49994] VGAM1437 gene encodes a VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1437 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1437 precursor RNA is designated SEQ ID:1423, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1423 is located at position 26 relative to the genome of Potato Virus A.

[49995] VGAM1437 precursor RNA folds onto itself, forming VGAM1437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[49996] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1437 folded precursor RNA into VGAM1437 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1437 RNA is designated SEQ ID:4148, and is provided hereinbelow with reference to the sequence listing part.

[49997] VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1437 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[49998] VGAM1437 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1437 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1437 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[49999] The complementary binding of VGAM1437 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1437 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1437 host target RNA into VGAM1437 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50000] It is appreciated that VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1437 host target genes. The mRNA of each one of this plurality of VGAM1437 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1437 RNA, herein designated VGAM RNA, and which when bound by VGAM1437 RNA causes inhibition of translation of respective one or more VGAM1437 host target proteins.

[50001] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1437 gene, herein designated VGAM GENE, on one or more VGAM1437 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50002] It is yet further appreciated that a function of VGAM1437 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1437 include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGAM1437 correlate with, and may be deduced from, the identity of the host target genes which VGAM1437 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50003] Nucleotide sequences of the VGAM1437 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1437 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1437 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1437 are further described hereinbelow with reference to Table 1.

[50004] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1437 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1437 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50005] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1437 gene, herein designated VGAM is inhibition of expression of VGAM1437 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1437 correlate with, and may be deduced from, the identity of the target genes which VGAM1437 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50006] Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM_006730) is a VGAM1437 host target gene. DNASE1L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DNASE1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNASE1L1 BINDING SITE, designated SEQ

ID:13568, to the nucleotide sequence of VGAM1437 RNA, herein designated VGAM RNA, also designated SEQ ID:4148.

[50007] A function of VGAM1437 is therefore inhibition of Deoxyribonuclease I-like 1 (DNASE1L1, Accession NM_006730), a gene which seems to be involved in cell death. Accordingly, utilities of VGAM1437 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNASE1L1. The function of DNASE1L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885.Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043) is another VGAM1437 host target gene. SLC6A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A6 BINDING SITE, designated SEQ ID:9002, to the nucleotide sequence of VGAM1437 RNA, herein designated VGAM RNA, also designated SEQ

ID:4148.

[50008] Another function of VGAM1437 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043), a gene which transports taurine and other beta-amino acids like beta-alanine. Accordingly, utilities of VGAM1437 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A6. The function of SLC6A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1438 (VGAM1438) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50009] VGAM1438 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1438 was detected is described hereinabove with reference to Figs. 1–8.

[50010] VGAM1438 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic

Necrosis Virus. VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50011] VGAM1438 gene encodes a VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1438 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1438 precursor RNA is designated SEQ ID:1424, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1424 is located at position 7374 relative to the genome of Bean Common Mosaic Necrosis Virus.

[50012] VGAM1438 precursor RNA folds onto itself, forming VGAM1438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50013] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1438 folded precursor RNA into VGAM1438 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1438 RNA is designated SEQ ID:4149, and is provided hereinbelow with reference to the sequence listing part.

[50014] VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1438 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50015] VGAM1438 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1438 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1438 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50016] The complementary binding of VGAM1438 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1438 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1438 host target RNA into VGAM1438 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50017] It is appreciated that VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1438 host target genes. The mRNA of each one of this plurality of VGAM1438 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1438 RNA, herein designated VGAM RNA, and which when bound by VGAM1438 RNA causes inhibition of translation of respective one or more VGAM1438 host target proteins.

[50018] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1438 gene, herein designated VGAM GENE, on one or more VGAM1438 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50019] It is yet further appreciated that a function of VGAM1438 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1438 correlate with, and may be deduced from, the identity of the host target genes which VGAM1438 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50020] Nucleotide sequences of the VGAM1438 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1438 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1438 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1438 are further described hereinbelow with reference to Table 1.

[50021] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1438 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1438 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50022] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1438 gene, herein designated VGAM is inhibition of expression of VGAM1438 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1438 correlate with, and may be deduced from, the identity of the target genes which VGAM1438 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50023] Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082) is a VGAM1438 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5532, to the nu-

cleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, also designated SEQ ID:4149.

[50024] A function of VGAM1438 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082). Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. GCN1 General Control of Amino-acid Synthesis 1-like 1 (yeast) (GCN1L1, Accession XM_045792) is another VGAM1438 host target gene. GCN1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GCN1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCN1L1 BINDING SITE, designated SEQ ID:34567, to the nucleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, also designated SEQ ID:4149.

[50025] Another function of VGAM1438 is therefore inhibition of GCN1 General Control of Amino-acid Synthesis 1-like 1 (yeast) (GCN1L1, Accession XM_045792), a gene which performs an EF3-related function on the ribosome by regulating GCN2 kinase activity. Accordingly, utilities of

VGAM1438 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCN1L1. The function of GCN1L1 has been established by previous studies. In *S. cerevisiae*, amino acid starvation causes increased transcription of genes encoding enzymes involved in amino acid biosynthesis. This process, known as general amino acid control, requires the phosphorylation of translation initiation factor eIF2 (see OMIM Ref. No. 603907) by protein kinase GCN2 and subsequent derepression of GCN4, a transcriptional activator that binds to the promoter of genes subject to the general control. Two other proteins, GCN1 and GCN20, are required for the activation of GCN2. Working with yeast GCN proteins, Marton et al. (1997) found that despite the presence of multiple hydrophobic regions indicating a putative transmembrane domain, GCN1 is located throughout the cytoplasm. The N-terminal region of GCN20 interacts with an internal segment of GCN1 that shows sequence similarity to translation elongation factor EF3 (see OMIM Ref. No. 603917). Both GCN1 and GCN20 stably interact with translating 80S ribosomes. Whereas GCN1 could bind to ribosomes independently of GCN20, its functions on polysomes were largely dependent on the ATP-binding

cassette of GCN20. By EST database searching for sequences related to GCN1, Marton et al. (1997) identified partial cDNAs of human GCN1L1. The portion of GCN1L1 that is highly conserved with yeast GCN1 also shows sequence similarity to yeast EF3. This conserved domain supports the hypothesis that GCN1L1 performs an EF3-related function on the ribosome by regulating GCN2 kinase activity.

[50026] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50027] Marton, M. J.; Vazquez de Aldana, C. R.; Qiu, H.; Chakraborty, K.; Hinnebusch, A. G. : Evidence that GCN1 and GCN20, translational regulators of GCN4, function on elongating ribosomes in activation of eIF2- α kinase GCN2. *Molec. Cell. Biol.* 17: 4474-4489, 1997. ; and

[50028] Nagase, T.; Seki, N.; Ishikawa, K.; Ohira, M.; Kwarabayasi, Y.; Ohara, O.; Tanaka, A.; Kotani, H.; Miyajima, N.; Nomura, N. : Prediction of the coding sequences of unidentified human g.

[50029] Further studies establishing the function and utilities of GCN1L1 are found in John Hopkins OMIM database record ID 605614, and in cited publications numbered 677 and

9379 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tumor Necrosis Factor Receptor Superfamily, Member 10b (TNFRSF10B, Accession NM_003842) is another VGAM1438 host target gene. TNFRSF10B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF10B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF10B BINDING SITE, designated SEQ ID:9934, to the nucleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, also designated SEQ ID:4149.

[50030] Another function of VGAM1438 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 10b (TNFRSF10B, Accession NM_003842), a gene which forms complex that induces apoptosis. Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF10B. The function of TNFRSF10B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM400. Enabled Homolog (Drosophila)

(ENAH, Accession NM_018212) is another VGAM1438 host target gene. ENAH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ENAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAH BINDING SITE, designated SEQ ID:20123, to the nucleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, also designated SEQ ID:4149.

[50031] Another function of VGAM1438 is therefore inhibition of Enabled Homolog (Drosophila) (ENAH, Accession NM_018212). Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAH. Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815) is another VGAM1438 host target gene. SLC5A7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC5A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC5A7 BINDING SITE, designated SEQ

ID:22388, to the nucleotide sequence of VGAM1438 RNA, herein designated VGAM RNA, also designated SEQ ID:4149.

[50032] Another function of VGAM1438 is therefore inhibition of Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815). Accordingly, utilities of VGAM1438 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC5A7. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1439 (VGAM1439) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50033] VGAM1439 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1439 was detected is described hereinabove with reference to Figs. 1–8.

[50034] VGAM1439 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Necrosis Virus. VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene con-

tained in the human genome.

[50035] VGAM1439 gene encodes a VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1439 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1439 precursor RNA is designated SEQ ID:1425, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1425 is located at position 4013 relative to the genome of Bean Common Mosaic Necrosis Virus.

[50036] VGAM1439 precursor RNA folds onto itself, forming VGAM1439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50037] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1439 folded precursor RNA into VGAM1439 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1439 RNA is designated SEQ ID:4150, and is provided hereinbelow with reference to the sequence listing part.

[50038] VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1439 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50039] VGAM1439 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1439 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1439 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50040] The complementary binding of VGAM1439 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1439 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1439 host target RNA into VGAM1439 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50041] It is appreciated that VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1439 host target genes. The mRNA of each one of this plurality of VGAM1439 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1439 RNA, herein designated VGAM RNA, and which when bound by VGAM1439 RNA causes inhibition of translation of respective one or more VGAM1439 host target proteins.

[50042] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1439 gene, herein designated VGAM GENE, on one or more VGAM1439 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50043] It is yet further appreciated that a function of VGAM1439 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1439 correlate with, and may be deduced from, the identity of the host target genes which VGAM1439 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50044] Nucleotide sequences of the VGAM1439 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1439 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1439 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1439 are further described hereinbelow with reference to Table 1.

[50045] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1439 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1439 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50046] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1439 gene, herein designated VGAM is inhibition of expression of VGAM1439 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1439 correlate with, and may be deduced from, the identity of the target genes which VGAM1439 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50047] Ras Homolog Gene Family, Member I (ARHI, Accession NM_004675) is a VGAM1439 host target gene. ARHI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHI BINDING SITE, designated SEQ ID:11043, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50048] A function of VGAM1439 is therefore inhibition of Ras Homolog Gene Family, Member I (ARHI, Accession NM_004675), a gene which is a Ras-related GTP-binding protein, member I; overexpression suppresses tumors. Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHI. The function of ARHI has been established by previous studies. The Ras (see OMIM Ref. No. HRAS; 190020) superfamily of protooncogenes is among the most commonly activated in a number of cancers, including breast and ovarian tumors. By differential display PCR and by screening a normal ovarian epithelial cell cDNA library, Yu et al. (1999) identified a cDNA encoding ARHI, which they termed NOEY2. Sequence analysis predicted that the 229-amino acid ARHI protein shares 54% amino acid homology with HRAS and 56 to 62% homology with RAS-related proteins (e.g., RAP1A; 179520). ARHI contains a highly conserved GTP-binding domain, a putative effector domain distinct from that of RAS and RAP proteins, and a C-terminal membrane localization motif. Northern blot analysis detected a 1.9-kb ARHI transcript in all normal breast and ovarian epithelial cell cultures tested, as well as in normal ovary, heart, liver, pancreas,

and brain. Expression was absent in nearly all breast and ovarian cancer cell lines and all primary ovarian cancer cell lines tested. Western blot analysis detected a 26-kD ARHI protein in all normal breast and ovarian cell lines but not in any breast and ovarian cancer cell lines tested. Expression of ARHI in breast and ovarian cancer cell lines but not in lung cancer cell lines led to growth inhibition. Stimulation of normal cell lines with growth factors led to decreased expression of ARHI as well as the cell growth inhibition-associated protein WAF1 (CDKN1A; 116899). Genomic sequence analysis demonstrated that the ARHI gene contains 2 exons. RFLP analysis of genomic DNA of informative families showed that ARHI is expressed monoallelically and is imprinted maternally. By PCR analysis of a genomic library and by FISH, Yu et al. (1999) mapped the ARHI gene to 1p31, a region that is frequently deleted in breast and ovarian cancer due to loss of heterozygosity; see 167000. To study the biologic function of the ARHI tumor suppressor gene, Xu et al. (2000) generated ARHI transgenic mice with ARHI expression driven by the cytomegalovirus promoter. Overexpression of ARHI in transgenic mice resulted in a decrease in body size and impaired development in multiple organs. Defects were par-

ticularly evident in fertility and postpartum lactation. The data suggested that ARHI is a negative regulator of murine growth as well as of the development and function of the breast and ovary.

[50049] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50050] Xu, F.; Xia, W.; Luo, R. Z.; Peng, H.; Zhao, S.; Dai, J.; Long, Y.; Zou, L.; Le, W.; Liu, J.; Parlow, A. F.; Hung, M.-C.; Bast, R. C., Jr.; Yu, Y. : The human ARHI tumor suppressor gene inhibits lactation and growth in transgenic mice. *Cancer Res.* 60: 4913–4920, 2000. ; and

[50051] Yu, Y.; Xu, F.; Peng, H.; Fang, X.; Zhao, S.; Li, Y.; Cuevas, B.; Kuo, W.-L.; Gray, J. W.; Siciliano, M.; Mills, G. B.; Bast, R. C., Jr. : NOEY2 (ARHI), an imprinted putative tumor sup.

[50052] Further studies establishing the function and utilities of ARHI are found in John Hopkins OMIM database record ID 605193, and in cited publications numbered 490 and 6607 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM_000132) is another VGAM1439 host target gene. F8 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by F8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F8 BINDING SITE, designated SEQ ID:5614, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50053] Another function of VGAM1439 is therefore inhibition of Coagulation Factor VIII, Procoagulant Component (hemophilia A) (F8, Accession NM_000132). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F8. Galanin Receptor 1 (GALR1, Accession NM_001480) is another VGAM1439 host target gene. GALR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GALR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALR1 BINDING SITE, designated SEQ ID:7218, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50054] Another function of VGAM1439 is therefore inhibition of Galanin Receptor 1 (GALR1, Accession NM_001480), a gene which plays a role in regulating ion transport. Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALR1. The function of GALR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1245. CAPN13 (Accession NM_144575) is another VGAM1439 host target gene. CAPN13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN13 BINDING SITE, designated SEQ ID:29379, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50055] Another function of VGAM1439 is therefore inhibition of CAPN13 (Accession NM_144575). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

CAPN13. FLJ22794 (Accession XM_166220) is another VGAM1439 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44026, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50056] Another function of VGAM1439 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. KIAA0212 (Accession NM_014674) is another VGAM1439 host target gene. KIAA0212 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0212, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0212 BINDING SITE, designated SEQ ID:16142, to the nucleotide sequence of VGAM1439 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4150.

[50057] Another function of VGAM1439 is therefore inhibition of KIAA0212 (Accession NM_014674). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0212. KIAA1317 (Accession XM_098368) is another VGAM1439 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41624, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50058] Another function of VGAM1439 is therefore inhibition of KIAA1317 (Accession XM_098368). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. KIAA1596 (Accession XM_048128) is another VGAM1439 host target gene. KIAA1596 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1596, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1596 BINDING SITE, designated SEQ ID:35120, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50059] Another function of VGAM1439 is therefore inhibition of KIAA1596 (Accession XM_048128). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1596. MGC21854 (Accession NM_052862) is another VGAM1439 host target gene. MGC21854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC21854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21854 BINDING SITE, designated SEQ ID:27448, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50060] Another function of VGAM1439 is therefore inhibition of MGC21854 (Accession NM_052862). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGC21854. Serine/threonine Kinase 17a (apoptosis-inducing) (STK17A, Accession NM_004760) is another VGAM1439 host target gene. STK17A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK17A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK17A BINDING SITE, designated SEQ ID:11153, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50061] Another function of VGAM1439 is therefore inhibition of Serine/threonine Kinase 17a (apoptosis-inducing) (STK17A, Accession NM_004760). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK17A. LOC148545 (Accession XM_086226) is another VGAM1439 host target gene. LOC148545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC148545 BINDING SITE, designated SEQ ID:38553, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50062] Another function of VGAM1439 is therefore inhibition of LOC148545 (Accession XM_086226). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148545. LOC219347 (Accession XM_167564) is another VGAM1439 host target gene. LOC219347 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219347 BINDING SITE, designated SEQ ID:44679, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50063] Another function of VGAM1439 is therefore inhibition of LOC219347 (Accession XM_167564). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219347. LOC51696 (Accession NM_016217) is an-

other VGAM1439 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18311, to the nucleotide sequence of VGAM1439 RNA, herein designated VGAM RNA, also designated SEQ ID:4150.

[50064] Another function of VGAM1439 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM1439 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1440 (VGAM1440) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50065] VGAM1440 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1440 was detected is de-

scribed hereinabove with reference to Figs. 1–8.

[50066] VGAM1440 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Necrosis Virus. VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50067] VGAM1440 gene encodes a VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1440 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1440 precursor RNA is designated SEQ ID:1426, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1426 is located at position 5334 relative to the genome of Bean Common Mosaic Necrosis Virus.

[50068] VGAM1440 precursor RNA folds onto itself, forming VGAM1440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA

gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50069] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1440 folded precursor RNA into VGAM1440 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 63%) nucleotide sequence of VGAM1440 RNA is designated SEQ ID:4151, and is provided hereinbelow with reference to the sequence listing part.

[50070] VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1440 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50071] VGAM1440 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites

located in untranslated regions of VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1440 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1440 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1440 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50072] The complementary binding of VGAM1440 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1440 host target RNA, herein designated VGAM

HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1440 host target RNA into VGAM1440 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50073] It is appreciated that VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1440 host target genes. The mRNA of each one of this plurality of VGAM1440 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1440 RNA, herein designated VGAM RNA, and which when bound by VGAM1440 RNA causes inhibition of translation of respective one or more VGAM1440 host target proteins.

[50074] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1440 gene, herein designated VGAM GENE, on one or more VGAM1440 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50075] It is yet further appreciated that a function of VGAM1440 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1440 correlate with, and may be deduced from, the identity of the host target genes which VGAM1440 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50076] Nucleotide sequences of the VGAM1440 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1440 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM1440 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1440 are further described hereinbelow with reference to Table 1.

[50077] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1440 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1440 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50078] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1440 gene, herein designated VGAM is inhibition of expression of VGAM1440 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1440 correlate with, and may be deduced from, the identity of the target genes which VGAM1440 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50079] Myeloma Overexpressed Gene (in a subset of t(11;14) Positive Multiple Myelomas) (MYEOV, Accession NM_138768) is a VGAM1440 host target gene. MYEOV BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MYEOV, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYEOV BINDING SITE, designated SEQ ID:28999, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50080] A function of VGAM1440 is therefore inhibition of Myeloma Overexpressed Gene (in a subset of t(11;14) Positive Multiple Myelomas) (MYEOV, Accession NM_138768), a gene which is encoded by MYELOMA OVEREXPRESSED GENE. Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYEOV. The function of MYEOV and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM471.Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na⁺/H⁺, amiloride sensitive) (SLC9A1, Accession XM_046881) is another VGAM1440 host target gene. SLC9A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC9A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A1 BINDING SITE, designated SEQ ID:34855, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50081] Another function of VGAM1440 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na⁺/H⁺, amiloride sensitive) (SLC9A1, Accession XM_046881), a gene which is involved in pH regulation to eliminate acids generated by active metabolism or to counter adverse environmental conditions. Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A1. The function of SLC9A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.DKFZP434B205 (Accession XM_059966) is another VGAM1440 host target gene. DKFZP434B205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434B205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZP434B205 BINDING SITE, designated SEQ ID:37127, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50082] Another function of VGAM1440 is therefore inhibition of DKFZP434B205 (Accession XM_059966). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B205. DKFZp434F142 (Accession NM_032254) is another VGAM1440 host target gene. DKFZp434F142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F142 BINDING SITE, designated SEQ ID:25992, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50083] Another function of VGAM1440 is therefore inhibition of DKFZp434F142 (Accession NM_032254). Accordingly, utilities of VGAM1440 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp434F142. FLJ14437 (Accession NM_032578) is another VGAM1440 host target gene. FLJ14437 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14437 BINDING SITE, designated SEQ ID:26310, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50084] Another function of VGAM1440 is therefore inhibition of FLJ14437 (Accession NM_032578). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14437. KIAA0522 (Accession XM_050404) is another VGAM1440 host target gene. KIAA0522 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0522 BINDING SITE, designated SEQ ID:35624, to the

nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50085] Another function of VGAM1440 is therefore inhibition of KIAA0522 (Accession XM_050404). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0522. MGC11287 (Accession NM_031464) is another VGAM1440 host target gene. MGC11287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11287 BINDING SITE, designated SEQ ID:25500, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50086] Another function of VGAM1440 is therefore inhibition of MGC11287 (Accession NM_031464). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11287. NPC1 (Niemann–Pick disease, type C1, gene)–like 1 (NPC1L1, Accession NM_013389) is another VGAM1440 host target gene. NPC1L1 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NPC1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPC1L1 BINDING SITE, designated SEQ ID:15039, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50087] Another function of VGAM1440 is therefore inhibition of NPC1 (Niemann–Pick disease, type C1, gene)–like 1 (NPC1L1, Accession NM_013389). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPC1L1. PP3501 (Accession NM_021731) is another VGAM1440 host target gene. PP3501 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PP3501, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP3501 BINDING SITE, designated SEQ ID:22330, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50088] Another function of VGAM1440 is therefore inhibition of PP3501 (Accession NM_021731). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP3501. LOC129676 (Accession XM_065341) is another VGAM1440 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37282, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50089] Another function of VGAM1440 is therefore inhibition of LOC129676 (Accession XM_065341). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129676. LOC145624 (Accession XM_096824) is another VGAM1440 host target gene. LOC145624 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145624, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145624 BINDING SITE, designated SEQ ID:40549, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50090] Another function of VGAM1440 is therefore inhibition of LOC145624 (Accession XM_096824). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145624. LOC146988 (Accession XM_097150) is another VGAM1440 host target gene. LOC146988 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146988 BINDING SITE, designated SEQ ID:40778, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50091] Another function of VGAM1440 is therefore inhibition of LOC146988 (Accession XM_097150). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146988. LOC147004 (Accession XM_097155) is another VGAM1440 host target gene. LOC147004 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147004 BINDING SITE, designated SEQ ID:40781, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50092] Another function of VGAM1440 is therefore inhibition of LOC147004 (Accession XM_097155). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147004. LOC148181 (Accession XM_086083) is another VGAM1440 host target gene. LOC148181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148181 BINDING SITE, designated SEQ ID:38481, to the nucleotide sequence of VGAM1440 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4151.

[50093] Another function of VGAM1440 is therefore inhibition of LOC148181 (Accession XM_086083). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148181. LOC148930 (Accession XM_086369) is another VGAM1440 host target gene. LOC148930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148930 BINDING SITE, designated SEQ ID:38622, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50094] Another function of VGAM1440 is therefore inhibition of LOC148930 (Accession XM_086369). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148930. LOC150630 (Accession XM_097931) is another VGAM1440 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150630, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41238, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50095] Another function of VGAM1440 is therefore inhibition of LOC150630 (Accession XM_097931). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. LOC151445 (Accession XM_045283) is another VGAM1440 host target gene. LOC151445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151445 BINDING SITE, designated SEQ ID:34420, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50096] Another function of VGAM1440 is therefore inhibition of LOC151445 (Accession XM_045283). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC151445. LOC152313 (Accession XM_098190) is another VGAM1440 host target gene. LOC152313 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152313 BINDING SITE, designated SEQ ID:41481, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50097] Another function of VGAM1440 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC154990 (Accession XM_088109) is another VGAM1440 host target gene. LOC154990 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC154990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154990 BINDING SITE, designated SEQ ID:39521, to

the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50098] Another function of VGAM1440 is therefore inhibition of LOC154990 (Accession XM_088109). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154990. LOC158476 (Accession XM_098955) is another VGAM1440 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:42002, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50099] Another function of VGAM1440 is therefore inhibition of LOC158476 (Accession XM_098955). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158476. LOC158835 (Accession XM_088683) is another VGAM1440 host target gene. LOC158835 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC158835, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158835 BINDING SITE, designated SEQ ID:39894, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50100] Another function of VGAM1440 is therefore inhibition of LOC158835 (Accession XM_088683). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158835. LOC196872 (Accession XM_113760) is another VGAM1440 host target gene. LOC196872 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196872 BINDING SITE, designated SEQ ID:42417, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50101] Another function of VGAM1440 is therefore inhibition of LOC196872 (Accession XM_113760). Accordingly, utilities

of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196872. LOC200261 (Accession XM_114172) is another VGAM1440 host target gene. LOC200261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200261 BINDING SITE, designated SEQ ID:42753, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50102] Another function of VGAM1440 is therefore inhibition of LOC200261 (Accession XM_114172). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200261. LOC222134 (Accession XM_168432) is another VGAM1440 host target gene. LOC222134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC222134 BINDING SITE, designated SEQ ID:45173, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50103] Another function of VGAM1440 is therefore inhibition of LOC222134 (Accession XM_168432). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222134. LOC254173 (Accession XM_173022) is another VGAM1440 host target gene. LOC254173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254173 BINDING SITE, designated SEQ ID:46286, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50104] Another function of VGAM1440 is therefore inhibition of LOC254173 (Accession XM_173022). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254173. LOC255975 (Accession XM_171083) is another VGAM1440 host target gene. LOC255975 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255975 BINDING SITE, designated SEQ ID:45891, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50105] Another function of VGAM1440 is therefore inhibition of LOC255975 (Accession XM_171083). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255975. LOC256529 (Accession XM_174314) is another VGAM1440 host target gene. LOC256529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256529 BINDING SITE, designated SEQ ID:46589, to the nucleotide sequence of VGAM1440 RNA, herein designated VGAM RNA, also designated SEQ ID:4151.

[50106] Another function of VGAM1440 is therefore inhibition of

LOC256529 (Accession XM_174314). Accordingly, utilities of VGAM1440 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256529. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1441 (VGAM1441) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50107] VGAM1441 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1441 was detected is described hereinabove with reference to Figs. 1-8.

[50108] VGAM1441 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Necrosis Virus. VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50109] VGAM1441 gene encodes a VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1441 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1441 precursor RNA is designated SEQ ID:1427, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1427 is located at position 5472 relative to the genome of Bean Common Mosaic Necrosis Virus.

- [50110] VGAM1441 precursor RNA folds onto itself, forming VGAM1441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [50111] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1441 folded precursor RNA into VGAM1441 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1441 RNA is designated SEQ ID:4152, and is provided hereinbelow with reference to the sequence listing part.

[50112] VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1441 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50113] VGAM1441 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1441 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1441 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[50114] The complementary binding of VGAM1441 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1441 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1441 host target RNA into VGAM1441 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50115] It is appreciated that VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1441 host target genes. The mRNA of each one of this plurality of VGAM1441 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1441 RNA, herein designated VGAM RNA, and which when bound by VGAM1441 RNA causes inhibition of translation of respective one or more VGAM1441 host target proteins.

[50116] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1441 gene, herein designated VGAM GENE, on one or more VGAM1441 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50117] It is yet further appreciated that a function of VGAM1441

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1441 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1441 correlate with, and may be deduced from, the identity of the host target genes which VGAM1441 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50118] Nucleotide sequences of the VGAM1441 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1441 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1441 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1441 are further described hereinbelow with reference to Table 1.

[50119] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1441 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1441 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50120] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1441 gene, herein designated VGAM is inhibition of expression of VGAM1441 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1441 correlate with, and may be deduced from, the identity of the target genes which VGAM1441 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50121] Thiopurine S-methyltransferase (TPMT, Accession NM_000367) is a VGAM1441 host target gene. TPMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TPMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPMT BINDING SITE, designated SEQ ID:5938, to the nucleotide sequence of VGAM1441 RNA, herein designated VGAM RNA, also designated SEQ ID:4152.

[50122] A function of VGAM1441 is therefore inhibition of Thiopurine S-methyltransferase (TPMT, Accession NM_000367), a gene which catalyzes the s-methylation of thiopurine drugs such as 6-mercaptopurine. Accordingly, utilities of VGAM1441 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with TPMT. The function of TPMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM682. Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM_005758) is another VGAM1441 host target gene. HNRPA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPA3 BINDING SITE, designated SEQ ID:12323, to the nucleotide sequence of VGAM1441 RNA, herein designated VGAM RNA, also designated SEQ ID:4152.

[50123] Another function of VGAM1441 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein A3 (HNRPA3, Accession NM_005758). Accordingly, utilities of VGAM1441 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPA3. LOC201564 (Accession XM_087368) is another VGAM1441 host target gene. LOC201564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC201564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201564 BINDING SITE, designated SEQ ID:39200, to the nucleotide sequence of VGAM1441 RNA, herein designated VGAM RNA, also designated SEQ ID:4152.

[50124] Another function of VGAM1441 is therefore inhibition of LOC201564 (Accession XM_087368). Accordingly, utilities of VGAM1441 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201564. LOC220988 (Accession XM_165561) is another VGAM1441 host target gene. LOC220988 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220988 BINDING SITE, designated SEQ ID:43682, to the nucleotide sequence of VGAM1441 RNA, herein designated VGAM RNA, also designated SEQ ID:4152.

[50125] Another function of VGAM1441 is therefore inhibition of LOC220988 (Accession XM_165561). Accordingly, utilities

of VGAM1441 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220988. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1442 (VGAM1442) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50126] VGAM1442 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1442 was detected is described hereinabove with reference to Figs. 1-8.

[50127] VGAM1442 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bean Common Mosaic Necrosis Virus. VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50128] VGAM1442 gene encodes a VGAM1442 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1442 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1442 precursor RNA is designated SEQ ID:1428, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1428 is located at position 7222 relative to the genome of Bean Common Mosaic Necrosis Virus.

[50129] VGAM1442 precursor RNA folds onto itself, forming VGAM1442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50130] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1442 folded precursor RNA into VGAM1442 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1442 RNA is designated SEQ ID:4153, and

is provided hereinbelow with reference to the sequence listing part.

[50131] VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1442 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50132] VGAM1442 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1442 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1442 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50133] The complementary binding of VGAM1442 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1442 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1442 host target RNA into VGAM1442 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50134] It is appreciated that VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1442 host target genes. The mRNA of each one of this plurality of VGAM1442 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1442 RNA, herein designated VGAM RNA, and which when bound by VGAM1442 RNA causes inhibition of translation of respective one or more VGAM1442 host target proteins.

[50135] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1442 gene, herein designated VGAM GENE, on one or more VGAM1442 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50136] It is yet further appreciated that a function of VGAM1442 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGAM1442 correlate with, and may be deduced from, the identity of the host target genes which VGAM1442 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50137] Nucleotide sequences of the VGAM1442 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1442 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1442 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1442 are further described hereinbelow with reference to Table 1.

[50138] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1442 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1442 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50139] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1442 gene, herein designated VGAM is inhibition of expression of VGAM1442 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1442 correlate with, and may be deduced from, the identity of the target genes which VGAM1442 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50140] Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990) is a VGAM1442 host target gene. GABRE BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GABRE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABRE BINDING SITE, designated SEQ ID:22530, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50141] A function of VGAM1442 is therefore inhibition of Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990), a gene which mediates neuronal inhibition by binding to the gaba/benzodiazepine receptor and opening an integral chloride

channel. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABRE. The function of GABRE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259. Inducible T-cell Co-stimulator (ICOS, Accession NM_012092) is another VGAM1442 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14389, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50142] Another function of VGAM1442 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18.NEBL (Accession NM_006393) is another VGAM1442 host target gene. NEBL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NEBL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEBL BINDING SITE, designated SEQ ID:13101, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50143] Another function of VGAM1442 is therefore inhibition of NEBL (Accession NM_006393). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEBL. Recombination Activating Gene 1 (RAG1, Accession NM_000448) is another VGAM1442 host target gene. RAG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RAG1 BINDING SITE, designated SEQ ID:6038, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50144] Another function of VGAM1442 is therefore inhibition of Recombination Activating Gene 1 (RAG1, Accession NM_000448). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAG1. Retinoblastoma-like 2 (p130) (RBL2, Accession NM_005611) is another VGAM1442 host target gene. RBL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBL2 BINDING SITE, designated SEQ ID:12132, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50145] Another function of VGAM1442 is therefore inhibition of Retinoblastoma-like 2 (p130) (RBL2, Accession NM_005611), a gene which may be a tumor suppressor. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with RBL2. The function of RBL2 has been established by previous studies. Mayol et al. (1993) cloned a retinoblastoma-related human gene, referred to as RB2, on the basis of sequence homology of the E1A-binding domain of the retinoblastoma gene (RB1; 180200). Structural homology with RB1 suggested a possible function of RB2 as a tumor suppressor gene. Yeung et al. (1993) mapped the gene to human chromosome 16q12.2 and rat chromosome 19, using fluorescence in situ hybridization and somatic hybrid cell analysis, respectively. Based on known syntenic relationships among human, rat and mouse, the data suggested that the mouse homolog resides on chromosome 8. Deletions of chromosome 16q have been found in several human neoplasms, including breast, ovarian, hepatic, and prostatic cancers, which supports the involvement of RB2 in human cancer as a tumor suppressor gene. This locus is symbolized RBL2 because it was identified after the gene on chromosome 20, which is symbolized RBL1 (OMIM Ref. No. 116957). RBL1 has a molecular weight of 107 kD; RBL2 has a molecular weight of about 120 kD.

[50146] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [50147] Baldi, A.; Boccia, V.; Claudio, P. P.; De Luca, A.; Giordano, A. : Genomic structure of the human retinoblastoma-related Rb2/p130 gene. Proc. Nat. Acad. Sci. 93: 4629–4632, 1996. ; and
- [50148] Mayol, X.; Grana, X.; Baldi, A.; Sang, N.; Hu, Q.; Giordano, A. : Cloning of a new member of the retinoblastoma gene family (pRb2) which binds to the E1A transforming domain. Oncogene.
- [50149] Further studies establishing the function and utilities of RBL2 are found in John Hopkins OMIM database record ID 180203, and in cited publications numbered 5666–5668 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SH3-domain Binding Protein 2 (SH3BP2, Accession NM_003023) is another VGAM1442 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2 BINDING SITE, designated SEQ ID:8944, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM

RNA, also designated SEQ ID:4153.

[50150] Another function of VGAM1442 is therefore inhibition of SH3-domain Binding Protein 2 (SH3BP2, Accession NM_003023). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP2. Tafazzin (cardiomyopathy, dilated 3A (X-linked); Endocardial Fibroelastosis 2; Barth Syndrome) (TAZ, Accession NM_000116) is another VGAM1442 host target gene. TAZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAZ BINDING SITE, designated SEQ ID:5587, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50151] Another function of VGAM1442 is therefore inhibition of Tafazzin (cardiomyopathy, dilated 3A (X-linked); Endocardial Fibroelastosis 2; Barth Syndrome) (TAZ, Accession NM_000116). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAZ. TIM3 (Accession

NM_032782) is another VGAM1442 host target gene. TIM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIM3 BINDING SITE, designated SEQ ID:26525, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50152] Another function of VGAM1442 is therefore inhibition of TIM3 (Accession NM_032782), a gene which regulates macrophage activation and enhances the severity of experimental autoimmune encephalomyelitis in mice. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIM3. The function of TIM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM909. Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394) is another VGAM1442 host target gene. ZNF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF10, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF10 BINDING SITE, designated SEQ ID:17694, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50153] Another function of VGAM1442 is therefore inhibition of Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394), a gene which may function as a transcriptional regulator. Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF10. The function of ZNF10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36. Zinc Finger Protein 35 (clone HF.10) (ZNF35, Accession NM_003420) is another VGAM1442 host target gene. ZNF35 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF35 BINDING SITE, designated SEQ ID:9465,

to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50154] Another function of VGAM1442 is therefore inhibition of Zinc Finger Protein 35 (clone HF.10) (ZNF35, Accession NM_003420). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF35. Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191) is another VGAM1442 host target gene. C1orf22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf22 BINDING SITE, designated SEQ ID:24838, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50155] Another function of VGAM1442 is therefore inhibition of Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf22. C20orf180 (Accession NM_018431) is another VGAM1442 host target

gene. C20orf180 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf180, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf180 BINDING SITE, designated SEQ ID:20495, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50156] Another function of VGAM1442 is therefore inhibition of C20orf180 (Accession NM_018431). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf180. FLJ10751 (Accession NM_018205) is another VGAM1442 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20094 and SEQ ID:20193 respectively, to the nucleotide sequence of

VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50157] Another function of VGAM1442 is therefore inhibition of FLJ10751 (Accession NM_018205). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM1442 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7860, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50158] Another function of VGAM1442 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. GS3955 (Accession NM_021643) is another VGAM1442 host target

gene. GS3955 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GS3955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GS3955 BINDING SITE, designated SEQ ID:22303, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50159] Another function of VGAM1442 is therefore inhibition of GS3955 (Accession NM_021643). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GS3955. KIAA0261 (Accession XM_042946) is another VGAM1442 host target gene. KIAA0261 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0261 BINDING SITE, designated SEQ ID:33833, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50160] Another function of VGAM1442 is therefore inhibition of KIAA0261 (Accession XM_042946). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0261. NDRG Family Member 4 (NDRG4, Accession NM_022910) is another VGAM1442 host target gene. NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2, designated SEQ ID:23214 and SEQ ID:21699 respectively, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50161] Another function of VGAM1442 is therefore inhibition of NDRG Family Member 4 (NDRG4, Accession NM_022910). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG4. RNAHP (Accession NM_007372) is another VGAM1442 host target gene. RNAHP BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by RNAHP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAHP BINDING SITE, designated SEQ ID:14300, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50162] Another function of VGAM1442 is therefore inhibition of RNAHP (Accession NM_007372). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNAHP. SEC15B (Accession XM_039570) is another VGAM1442 host target gene. SEC15B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SEC15B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC15B BINDING SITE, designated SEQ ID:33124, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50163] Another function of VGAM1442 is therefore inhibition of

SEC15B (Accession XM_039570). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC15B. Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM_133489) is another VGAM1442 host target gene. SLC26A10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC26A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A10 BINDING SITE, designated SEQ ID:28559, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50164] Another function of VGAM1442 is therefore inhibition of Solute Carrier Family 26, Member 10 (SLC26A10, Accession NM_133489). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A10. TU3A (Accession NM_007177) is another VGAM1442 host target gene. TU3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU3A, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU3A BINDING SITE, designated SEQ ID:14033, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50165] Another function of VGAM1442 is therefore inhibition of TU3A (Accession NM_007177). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TU3A. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023) is another VGAM1442 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27576, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50166] Another function of VGAM1442 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023). Accordingly, utilities of VGAM1442 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. LOC130612 (Accession XM_059461) is another VGAM1442 host target gene. LOC130612 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC130612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130612 BINDING SITE, designated SEQ ID:36999, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50167] Another function of VGAM1442 is therefore inhibition of LOC130612 (Accession XM_059461). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130612. LOC151195 (Accession XM_087125) is another VGAM1442 host target gene. LOC151195 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC151195 BINDING SITE, designated SEQ ID:39076, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50168] Another function of VGAM1442 is therefore inhibition of LOC151195 (Accession XM_087125). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151195. LOC152220 (Accession XM_098176) is another VGAM1442 host target gene. LOC152220 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152220 BINDING SITE, designated SEQ ID:41442, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50169] Another function of VGAM1442 is therefore inhibition of LOC152220 (Accession XM_098176). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152220. LOC196527 (Accession XM_113743) is another VGAM1442 host target gene. LOC196527 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196527 BINDING SITE, designated SEQ ID:42399, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50170] Another function of VGAM1442 is therefore inhibition of LOC196527 (Accession XM_113743). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196527. LOC197358 (Accession XM_113872) is another VGAM1442 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42510, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50171] Another function of VGAM1442 is therefore inhibition of

LOC197358 (Accession XM_113872). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC200734 (Accession XM_114286) is another VGAM1442 host target gene. LOC200734 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200734, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200734 BINDING SITE, designated SEQ ID:42840, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50172] Another function of VGAM1442 is therefore inhibition of LOC200734 (Accession XM_114286). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200734. LOC201164 (Accession XM_113904) is another VGAM1442 host target gene. LOC201164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC201164 BINDING SITE, designated SEQ ID:42530, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50173] Another function of VGAM1442 is therefore inhibition of LOC201164 (Accession XM_113904). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201164. LOC254085 (Accession XM_171189) is another VGAM1442 host target gene. LOC254085 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254085, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254085 BINDING SITE, designated SEQ ID:45971, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50174] Another function of VGAM1442 is therefore inhibition of LOC254085 (Accession XM_171189). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254085. LOC257117 (Accession XM_171238) is an-

other VGAM1442 host target gene. LOC257117 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257117 BINDING SITE, designated SEQ ID:46026, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50175] Another function of VGAM1442 is therefore inhibition of LOC257117 (Accession XM_171238). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257117. LOC257336 (Accession XM_171216) is another VGAM1442 host target gene. LOC257336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257336 BINDING SITE, designated SEQ ID:46003, to the nucleotide sequence of VGAM1442 RNA, herein designated VGAM RNA, also designated SEQ ID:4153.

[50176] Another function of VGAM1442 is therefore inhibition of LOC257336 (Accession XM_171216). Accordingly, utilities of VGAM1442 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257336. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1443 (VGAM1443) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50177] VGAM1443 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1443 was detected is described hereinabove with reference to Figs. 1–8.

[50178] VGAM1443 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus. VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50179] VGAM1443 gene encodes a VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1443 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1443 precursor RNA is designated SEQ ID:1429, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1429 is located at position 4259 relative to the genome of Pepper Mottle Virus.

- [50180] VGAM1443 precursor RNA folds onto itself, forming VGAM1443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [50181] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1443 folded precursor RNA into VGAM1443 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1443 RNA is designated SEQ ID:4154, and is provided hereinbelow with reference to the sequence listing part.

[50182] VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1443 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[50183] VGAM1443 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1443 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1443 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50184] The complementary binding of VGAM1443 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1443 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1443 host target RNA into VGAM1443 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50185] It is appreciated that VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1443 host target genes. The mRNA of each one of this plurality of VGAM1443 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1443 RNA, herein designated VGAM RNA, and which when bound by VGAM1443 RNA causes inhibition of translation of respective one or more VGAM1443 host target proteins.

[50186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1443 gene, herein designated VGAM GENE, on one or more VGAM1443 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50187] It is yet further appreciated that a function of VGAM1443 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1443 correlate with, and may be deduced from, the identity of the host target genes which VGAM1443 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50188] Nucleotide sequences of the VGAM1443 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1443 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1443 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1443 are further described hereinbelow with reference to Table 1.

[50189] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1443 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1443 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[50190] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1443 gene, herein designated VGAM is inhibition of expression of VGAM1443 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1443 correlate with, and may be deduced from, the identity of the target genes which VGAM1443 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50191] Nucleolar Protein Family A, Member 1 (H/ACA small nucleolar RNPs) (NOLA1, Accession NM_018983) is a VGAM1443 host target gene. NOLA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NOLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOLA1 BINDING SITE, designated SEQ ID:21053, to the nucleotide sequence of VGAM1443 RNA, herein designated VGAM RNA, also designated SEQ ID:4154.

[50192] A function of VGAM1443 is therefore inhibition of Nucleolar Protein Family A, Member 1 (H/ACA small nucleolar RNPs) (NOLA1, Accession NM_018983), a gene which as-

sociates with a only a subset of snrna's and is essential for growth. Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOLA1. The function of NOLA1 has been established by previous studies. Small nucleolar RNAs (snoRNAs) of the H/ACA class specify the sites of uridine-to-pseudouridine conversion. The H and ACA motifs are located in the hinge and tail, respectively, of a 2-domain hairpin-hinge-hairpin-tail structure. The uridine conversion process, together with the removal of the spacer region and the 2-prime-O-methylation of ribose groups, which is carried out by snoRNAs of the C/D class, is required for the generation of functional rRNAs. See Tollervey and Kiss (1997) for further information. By cell fractionation and competition assays, Dragon et al. (2000) showed that the 3-prime terminal hairpin of U17 cleavage RNA (see OMIM Ref. No. 603238) and telomerase RNA can form a ribonucleoprotein (RNP) in association with RNAs and 4 proteins (60, 29, 23, and 14 kD) of the H/ACA class. By EST database searching and probing a Burkitt lymphoma cDNA library, Dragon et al. (2000) obtained a cDNA encoding NOLA1, which they called GAR1 after its yeast homolog. The deduced 217-amino acid NOLA1 pro-

tein contains a core domain that is flanked by glycine- and arginine-rich (GAR) domains, which compose half of the sequence. Western blot analysis showed expression of a 28-kD protein, higher than the calculated mass of 23 kD. Immunoprecipitation analysis demonstrated that NOLA1 is a subunit of H/ACA snoRNPs and telomerase, but it is not required for H/ACA protein assembly. Dragon et al. (2000) proposed that the 23- and 14-kD H/ACA proteins represent the human homologs of the yeast Nhp2 (NOLA2; 606470) and Nop10 (NOLA3; 606471) proteins.

[50193] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50194] Dragon, F.; Pogacic, V.; Filipowicz, W. : In vitro assembly of human H/ACA small nucleolar RNPs reveals unique features of U17 and telomerase RNAs. *Molec. Cell. Biol.* 20: 3037–3048, 2000. ; and

[50195] Tollervey, D.; Kiss, T. : Function and synthesis of small nucleolar RNAs. *Curr. Opin. Cell Biol.* 9: 337–342, 1997.

[50196] Further studies establishing the function and utilities of NOLA1 are found in John Hopkins OMIM database record ID 606468, and in cited publications numbered

4534–4535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine/arginine Repetitive Matrix 1 (SRRM1, Accession NM_005839) is another VGAM1443 host target gene. SRRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRRM1 BINDING SITE, designated SEQ ID:12449, to the nucleotide sequence of VGAM1443 RNA, herein designated VGAM RNA, also designated SEQ ID:4154.

[50197] Another function of VGAM1443 is therefore inhibition of Serine/arginine Repetitive Matrix 1 (SRRM1, Accession NM_005839). Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRRM1. CSL4 (Accession NM_016046) is another VGAM1443 host target gene. CSL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of CSL4 BINDING SITE, designated SEQ ID:18125, to the nucleotide sequence of VGAM1443 RNA, herein designated VGAM RNA, also designated SEQ ID:4154.

[50198] Another function of VGAM1443 is therefore inhibition of CSL4 (Accession NM_016046). Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSL4. PRMT6 (Accession NM_018137) is another VGAM1443 host target gene. PRMT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRMT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRMT6 BINDING SITE, designated SEQ ID:19935, to the nucleotide sequence of VGAM1443 RNA, herein designated VGAM RNA, also designated SEQ ID:4154.

[50199] Another function of VGAM1443 is therefore inhibition of PRMT6 (Accession NM_018137). Accordingly, utilities of VGAM1443 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRMT6. Fig. 1 further provides a conceptual description of a novel

bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1444 (VGAM1444) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50200] VGAM1444 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1444 was detected is described hereinabove with reference to Figs. 1–8.

[50201] VGAM1444 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus. VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50202] VGAM1444 gene encodes a VGAM1444 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1444 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1444 precursor RNA is designated SEQ ID:1430, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1430 is located at position 4768 relative to the

genome of Pepper Mottle Virus.

[50203] VGAM1444 precursor RNA folds onto itself, forming VGAM1444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50204] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1444 folded precursor RNA into VGAM1444 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1444 RNA is designated SEQ ID:4155, and is provided hereinbelow with reference to the sequence listing part.

[50205] VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1444 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[50206] VGAM1444 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1444 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1444 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50207] The complementary binding of VGAM1444 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1444 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1444 host target RNA into VGAM1444 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50208] It is appreciated that VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1444 host target genes. The mRNA of each one of this plurality of VGAM1444 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1444 RNA, herein designated VGAM RNA, and which when bound by VGAM1444 RNA causes inhibition of translation of respective one or more VGAM1444 host target proteins.

[50209] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1444 gene, herein designated VGAM GENE, on one or more VGAM1444 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50210] It is yet further appreciated that a function of VGAM1444 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1444

correlate with, and may be deduced from, the identity of the host target genes which VGAM1444 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50211] Nucleotide sequences of the VGAM1444 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1444 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1444 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1444 are further described hereinbelow with reference to Table 1.

[50212] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1444 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1444 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50213] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1444 gene, herein designated VGAM is inhibition of expression of VGAM1444 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1444 correlate with, and may be deduced

from, the identity of the target genes which VGAM1444 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50214] APG5 Autophagy 5-like (*S. cerevisiae*) (APG5L, Accession NM_004849) is a VGAM1444 host target gene. APG5L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APG5L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APG5L BINDING SITE, designated SEQ ID:11263, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50215] A function of VGAM1444 is therefore inhibition of APG5 Autophagy 5-like (*S. cerevisiae*) (APG5L, Accession NM_004849), a gene which conjugates to apg12 and associates with isolation membrane to form cup-shaped isolation membrane and autophagosome. Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APG5L. The function of APG5L and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM492. Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011) is another VGAM1444 host target gene. SOCS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOCS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOCS5 BINDING SITE, designated SEQ ID:15226, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50216] Another function of VGAM1444 is therefore inhibition of Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOCS5. X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 2 (XRCC2, Accession NM_005431) is another VGAM1444 host target gene. XRCC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of XRCC2 BINDING SITE, designated SEQ ID:11902, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50217] Another function of VGAM1444 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 2 (XRCC2, Accession NM_005431), a gene which involves in the homologous recombination repair (hrr) pathway of double-stranded dna. Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC2. The function of XRCC2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM241. Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940) is another VGAM1444 host target gene. C21orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf6 BINDING SITE, designated SEQ ID:18856, to the nucleotide

sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50218] Another function of VGAM1444 is therefore inhibition of Chromosome 21 Open Reading Frame 6 (C21orf6, Accession NM_016940). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf6. FLJ11259 (Accession NM_018370) is another VGAM1444 host target gene. FLJ11259 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11259 BINDING SITE, designated SEQ ID:20389, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50219] Another function of VGAM1444 is therefore inhibition of FLJ11259 (Accession NM_018370). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11259. KIAA0514 (Accession NM_014696) is another VGAM1444 host target gene. KIAA0514 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0514 BINDING SITE, designated SEQ ID:16210, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50220] Another function of VGAM1444 is therefore inhibition of KIAA0514 (Accession NM_014696). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0514. KIAA1317 (Accession XM_098368) is another VGAM1444 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41627, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50221] Another function of VGAM1444 is therefore inhibition of

KIAA1317 (Accession XM_098368). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. Zinc Finger Protein 300 (ZNF300, Accession NM_052860) is another VGAM1444 host target gene. ZNF300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF300 BINDING SITE, designated SEQ ID:27441, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50222] Another function of VGAM1444 is therefore inhibition of Zinc Finger Protein 300 (ZNF300, Accession NM_052860). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF300. LOC255018 (Accession XM_173504) is another VGAM1444 host target gene. LOC255018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255018, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255018 BINDING SITE, designated SEQ ID:46546, to the nucleotide sequence of VGAM1444 RNA, herein designated VGAM RNA, also designated SEQ ID:4155.

[50223] Another function of VGAM1444 is therefore inhibition of LOC255018 (Accession XM_173504). Accordingly, utilities of VGAM1444 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255018. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1445 (VGAM1445) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50224] VGAM1445 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1445 was detected is described hereinabove with reference to Figs. 1–8.

[50225] VGAM1445 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus.

VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50226] VGAM1445 gene encodes a VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1445 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1445 precursor RNA is designated SEQ ID:1431, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1431 is located at position 5583 relative to the genome of Pepper Mottle Virus.

[50227] VGAM1445 precursor RNA folds onto itself, forming VGAM1445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50228] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1445 folded precursor RNA into VGAM1445 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1445 RNA is designated SEQ ID:4156, and is provided hereinbelow with reference to the sequence listing part.

[50229] VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1445 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50230] VGAM1445 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1445 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1445 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50231] The complementary binding of VGAM1445 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1445 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1445 host target RNA into VGAM1445 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50232] It is appreciated that VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1445 host target genes. The mRNA of each one of this plurality of VGAM1445 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1445 RNA, herein designated VGAM RNA, and which when bound by VGAM1445 RNA causes inhibition of translation of respective one or more VGAM1445 host target proteins.

[50233] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1445 gene, herein designated VGAM GENE, on one or more VGAM1445 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50234] It is yet further appreciated that a function of VGAM1445 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1445 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1445 correlate with, and may be deduced from, the identity of the host target genes which VGAM1445 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50235] Nucleotide sequences of the VGAM1445 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1445 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1445 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1445 are further described hereinbelow with reference to Table 1.

[50236] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1445 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1445 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50237] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1445 gene, herein designated VGAM is inhibition of expression of VGAM1445 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1445 correlate with, and may be deduced from, the identity of the target genes which VGAM1445 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50238] Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM_168542) is a VGAM1445 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45225,

to the nucleotide sequence of VGAM1445 RNA, herein designated VGAM RNA, also designated SEQ ID:4156.

[50239] A function of VGAM1445 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM1445 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174.KIAA0218 (Accession NM_014760) is another VGAM1445 host target gene. KIAA0218 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0218 BINDING SITE, designated SEQ ID:16515, to the nucleotide sequence of VGAM1445 RNA, herein designated VGAM RNA, also designated SEQ ID:4156.

[50240] Another function of VGAM1445 is therefore inhibition of

KIAA0218 (Accession NM_014760). Accordingly, utilities of VGAM1445 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0218. LOC153688 (Accession XM_098416) is another VGAM1445 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41657, to the nucleotide sequence of VGAM1445 RNA, herein designated VGAM RNA, also designated SEQ ID:4156.

[50241] Another function of VGAM1445 is therefore inhibition of LOC153688 (Accession XM_098416). Accordingly, utilities of VGAM1445 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1446 (VGAM1446) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[50242] VGAM1446 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1446 was detected is described hereinabove with reference to Figs. 1–8.

[50243] VGAM1446 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus. VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50244] VGAM1446 gene encodes a VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1446 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1446 precursor RNA is designated SEQ ID:1432, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1432 is located at position 3107 relative to the genome of Pepper Mottle Virus.

[50245] VGAM1446 precursor RNA folds onto itself, forming VGAM1446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50246] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1446 folded precursor RNA into VGAM1446 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1446 RNA is designated SEQ ID:4157, and is provided hereinbelow with reference to the sequence listing part.

[50247] VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1446 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50248] VGAM1446 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1446 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1446 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[50249] The complementary binding of VGAM1446 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1446 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1446 host target RNA into VGAM1446 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50250] It is appreciated that VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1446 host target genes. The mRNA of each one of this plurality of VGAM1446 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1446 RNA, herein designated VGAM RNA, and which when bound by VGAM1446 RNA causes inhibition of translation of respective one or more VGAM1446 host target proteins.

[50251] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1446 gene, herein designated VGAM GENE, on one

or more VGAM1446 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50252] It is yet further appreciated that a function of VGAM1446 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1446 correlate with, and may be deduced from, the identity of the host target genes which VGAM1446 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50253] Nucleotide sequences of the VGAM1446 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1446 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1446 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1446 are further described hereinbelow with reference to Table 1.

[50254] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1446 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1446 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50255] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1446 gene, herein designated VGAM is inhibition of expression of VGAM1446 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1446 correlate with, and may be deduced from, the identity of the target genes which VGAM1446 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50256] Fibulin 5 (FBLN5, Accession NM_006329) is a VGAM1446

host target gene. FBLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN5 BINDING SITE, designated SEQ ID:13024, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50257] A function of VGAM1446 is therefore inhibition of Fibulin 5 (FBLN5, Accession NM_006329), a gene which promotes adhesion of endothelial cells through interaction of integrins and the rgd motif. Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN5. The function of FBLN5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1127. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM_006496) is another VGAM1446 host target gene. GNAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

GNAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI3 BINDING SITE, designated SEQ ID:13238, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50258] Another function of VGAM1446 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM_006496), a gene which stimulates receptor regulated K⁺-channels. Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI3. The function of GNAI3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM45. Interleukin Enhancer Binding Factor 1 (ILF1, Accession NM_004514) is another VGAM1446 host target gene. ILF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ILF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of ILF1 BINDING SITE, designated SEQ ID:10843, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50259] Another function of VGAM1446 is therefore inhibition of Interleukin Enhancer Binding Factor 1 (ILF1, Accession NM_004514), a gene which binds to nfat-like motifs (purine-rich) in the hiv-1 long terminal repeat and in the il-2 promoter. Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ILF1. The function of ILF1 has been established by previous studies. Li et al. (1991) cloned a cellular factor, known as ILF (for interleukin enhancer-binding factor), from both HeLa and Jurkat cDNA libraries. ILF binds to purine-rich regulatory motifs in the HIV-1 LTR (long terminal repeat) and to interleukin-2 promoter (IL2; 147680). Further analysis of the ILF gene demonstrated the existence of 2 mRNA species, both of which encode proteins containing the 'forkhead' DNA binding domain (Li et al., 1992). By analysis of a panel of mouse/human somatic cell hybrids followed by radioactive in situ hybridization, Li et al. (1992) demonstrated that the ILF gene is located on 17q25, which is a site of

chromosomal translocations in some cases of human acute myelogenous leukemia. HTLF (OMIM Ref. No. 143089) is another 'forkhead' domain DNA binding protein, which is located on 2p22-p16

[50260] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50261] Li, C.; Lai, C.; Sigman, D. S.; Gaynor, R. B. : Cloning of a cellular factor, interleukin binding factor, that binds to NFAT-like motifs in the human immunodeficiency virus long terminal repeat. Proc. Nat. Acad. Sci. 88: 7739-7743, 1991. ; and

[50262] Li, C.; Lysis, A. J.; Sparkes, R.; Nirula, A.; Gaynor, R. : Characterization and chromosomal mapping of the gene encoding the cellular DNA binding protein ILF. Genomics 13: 665-671, 1992.

[50263] Further studies establishing the function and utilities of ILF1 are found in John Hopkins OMIM database record ID 147685, and in cited publications numbered 5246-5247 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355) is another VGAM1446 host target

gene. MPP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP2 BINDING SITE, designated SEQ ID:30080, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50264] Another function of VGAM1446 is therefore inhibition of Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP2. Myotubular Myopathy 1 (MTM1, Accession NM_000252) is another VGAM1446 host target gene. MTM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTM1 BINDING SITE, designated SEQ ID:5790, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50265] Another function of VGAM1446 is therefore inhibition of Myotubular Myopathy 1 (MTM1, Accession NM_000252). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTM1. Dynein, Cytoplasmic, Light Intermediate Polypeptide 1 (DNCLI1, Accession XM_003119) is another VGAM1446 host target gene. DNCLI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNCLI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNCLI1 BINDING SITE, designated SEQ ID:29927, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50266] Another function of VGAM1446 is therefore inhibition of Dynein, Cytoplasmic, Light Intermediate Polypeptide 1 (DNCLI1, Accession XM_003119). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNCLI1. F-box Only Protein 21 (FBXO21, Accession NM_033624) is another VGAM1446 host target gene.

FBXO21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO21 BINDING SITE, designated SEQ ID:27325, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50267] Another function of VGAM1446 is therefore inhibition of F-box Only Protein 21 (FBXO21, Accession NM_033624). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO21. KIAA1615 (Accession XM_044021) is another VGAM1446 host target gene. KIAA1615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1615 BINDING SITE, designated SEQ ID:34086, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ

ID:4157.

[50268] Another function of VGAM1446 is therefore inhibition of KIAA1615 (Accession XM_044021). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1615. Paternally Expressed 10 (PEG10, Accession NM_015068) is another VGAM1446 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17432, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50269] Another function of VGAM1446 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM_015068). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. LOC155435 (Accession XM_088257) is another VGAM1446 host target gene. LOC155435 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LOC155435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155435 BINDING SITE, designated SEQ ID:39568, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50270] Another function of VGAM1446 is therefore inhibition of LOC155435 (Accession XM_088257). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155435. LOC160717 (Accession XM_090457) is another VGAM1446 host target gene. LOC160717 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160717 BINDING SITE, designated SEQ ID:40008, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50271] Another function of VGAM1446 is therefore inhibition of

LOC160717 (Accession XM_090457). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160717. LOC222865 (Accession XM_167242) is another VGAM1446 host target gene. LOC222865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222865 BINDING SITE, designated SEQ ID:44621, to the nucleotide sequence of VGAM1446 RNA, herein designated VGAM RNA, also designated SEQ ID:4157.

[50272] Another function of VGAM1446 is therefore inhibition of LOC222865 (Accession XM_167242). Accordingly, utilities of VGAM1446 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222865. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1447 (VGAM1447) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[50273] VGAM1447 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1447 was detected is described hereinabove with reference to Figs. 1–8.

[50274] VGAM1447 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus. VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50275] VGAM1447 gene encodes a VGAM1447 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1447 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1447 precursor RNA is designated SEQ ID:1433, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1433 is located at position 1681 relative to the genome of Pepper Mottle Virus.

[50276] VGAM1447 precursor RNA folds onto itself, forming VGAM1447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50277] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1447 folded precursor RNA into VGAM1447 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1447 RNA is designated SEQ ID:4158, and is provided hereinbelow with reference to the sequence listing part.

[50278] VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1447 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50279] VGAM1447 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1447 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1447 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[50280] The complementary binding of VGAM1447 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1447 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1447 host target RNA into VGAM1447 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50281] It is appreciated that VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1447 host target genes. The mRNA of each one of this plurality of VGAM1447 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1447 RNA, herein designated VGAM RNA, and which when bound by VGAM1447 RNA causes inhibition of translation of respective one or more VGAM1447 host target proteins.

[50282] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1447 gene, herein designated VGAM GENE, on one

or more VGAM1447 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50283] It is yet further appreciated that a function of VGAM1447 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1447 correlate with, and may be deduced from, the identity of the host target genes which VGAM1447 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50284] Nucleotide sequences of the VGAM1447 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1447 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1447 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1447 are further described hereinbelow with reference to Table 1.

[50285] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1447 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1447 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50286] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1447 gene, herein designated VGAM is inhibition of expression of VGAM1447 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1447 correlate with, and may be deduced from, the identity of the target genes which VGAM1447 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50287] A Disintegrin-like and Metalloprotease (reprolysin type)

with Thrombospondin Type 1 Motif, 1 (ADAMTS1, Accession NM_006988) is a VGAM1447 host target gene.

ADAMTS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADAMTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS1 BINDING SITE, designated SEQ ID:13853, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50288] A function of VGAM1447 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 1 (ADAMTS1, Accession NM_006988). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS1. Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286) is another VGAM1447 host target gene. AQP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of AQP6 BINDING SITE, designated SEQ ID:27618, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50289] Another function of VGAM1447 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286), a gene which participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM340. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_004007) is another VGAM1447 host target gene. DMD BINDING SITE1 and DMD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 and DMD

BINDING SITE2, designated SEQ ID:10160 and SEQ ID:10174 respectively, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50290] Another function of VGAM1447 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_004007), a gene which muscular dystrophy . Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228) is another VGAM1447 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11727, to the nucleotide sequence of

VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50291] Another function of VGAM1447 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM229. Fatty-acid-Coenzyme A Ligase, Long-chain 5 (FACL5, Accession XM_034424) is another VGAM1447 host target gene. FACL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FACL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL5 BINDING SITE, designated SEQ ID:32108, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50292] Another function of VGAM1447 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 5 (FACL5, Accession XM_034424), a gene which may be involved in fatty acid metabolism; contains an AMP-binding domain. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL5. The function of FACL5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM357. GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491) is another VGAM1447 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:27843 and SEQ ID:14647 respectively, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50293] Another function of VGAM1447 is therefore inhibition of

GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53.IMP (inosine monophosphate) Dehydrogenase 1 (IMPDH1, Accession NM_000883) is another VGAM1447 host target gene. IMPDH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IMPDH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPDH1 BINDING SITE, designated SEQ ID:6578, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50294] Another function of VGAM1447 is therefore inhibition of IMP (inosine monophosphate) Dehydrogenase 1 (IMPDH1, Accession NM_000883). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with IM-PDH1. Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM_018658) is another VGAM1447 host target gene. KCNJ16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KCNJ16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ16 BINDING SITE, designated SEQ ID:20730, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50295] Another function of VGAM1447 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM_018658). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ16. N-acetylgalactosaminidase, Alpha- (NAGA, Accession NM_000262) is another VGAM1447 host target gene. NAGA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NAGA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of NAGA BINDING SITE, designated SEQ ID:5801, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50296] Another function of VGAM1447 is therefore inhibition of N-acetylgalactosaminidase, Alpha- (NAGA, Accession NM_000262). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAGA. Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM_009699) is another VGAM1447 host target gene. NRIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRIP1 BINDING SITE, designated SEQ ID:30120, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50297] Another function of VGAM1447 is therefore inhibition of Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM_009699), a gene which modulates transcriptional activation by the estrogen receptor. Accordingly, utilities of

VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRIP1. The function of NRIP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237) is another VGAM1447 host target gene. POU4F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU4F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU4F1 BINDING SITE, designated SEQ ID:12901, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50298] Another function of VGAM1447 is therefore inhibition of POU Domain, Class 4, Transcription Factor 1 (POU4F1, Accession NM_006237), a gene which plays a role in the regulation of specific gene expression within a subset of neuronal lineages. Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU4F1. The function

of POU4F1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1026. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184) is another VGAM1447 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31299, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50299] Another function of VGAM1447 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1. BMF (Accession NM_033503) is another VGAM1447 host target gene. BMF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BMF, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMF BINDING SITE, designated SEQ ID:27277, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50300] Another function of VGAM1447 is therefore inhibition of BMF (Accession NM_033503). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMF. Caspase 9, Apoptosis-related Cysteine Protease (CASP9, Accession NM_001229) is another VGAM1447 host target gene. CASP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CASP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP9 BINDING SITE, designated SEQ ID:6901, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50301] Another function of VGAM1447 is therefore inhibition of Caspase 9, Apoptosis-related Cysteine Protease (CASP9,

Accession NM_001229). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP9. Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM_086803) is another VGAM1447 host target gene. CECR7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CECR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR7 BINDING SITE, designated SEQ ID:38881, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50302] Another function of VGAM1447 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 7 (CECR7, Accession XM_086803). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR7. C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 9 (CLECSF9, Accession NM_014358) is another VGAM1447 host target gene. CLECSF9 BINDING SITE is HOST TARGET binding site found

in the 5' untranslated region of mRNA encoded by CLECSF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF9 BINDING SITE, designated SEQ ID:15688, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50303] Another function of VGAM1447 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 9 (CLECSF9, Accession NM_014358). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF9. CCR4-NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779) is another VGAM1447 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11177, to the nucleotide sequence of VGAM1447 RNA,

herein designated VGAM RNA, also designated SEQ ID:4158.

[50304] Another function of VGAM1447 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. DCOHM (Accession NM_032151) is another VGAM1447 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25850, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50305] Another function of VGAM1447 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM_030881) is another

VGAM1447 host target gene. DDX17 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DDX17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX17 BINDING SITE, designated SEQ ID:25155, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50306] Another function of VGAM1447 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 17, 72kDa (DDX17, Accession NM_030881). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX17. FLJ10242 (Accession NM_018036) is another VGAM1447 host target gene. FLJ10242 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10242 BINDING SITE, designated SEQ ID:19777, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM

RNA, also designated SEQ ID:4158.

[50307] Another function of VGAM1447 is therefore inhibition of FLJ10242 (Accession NM_018036). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10242. FLJ10936 (Accession NM_018279) is another VGAM1447 host target gene. FLJ10936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10936 BINDING SITE, designated SEQ ID:20271, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50308] Another function of VGAM1447 is therefore inhibition of FLJ10936 (Accession NM_018279). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10936. FLJ13614 (Accession NM_139076) is another VGAM1447 host target gene. FLJ13614 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13614, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13614 BINDING SITE, designated SEQ ID:29149, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50309] Another function of VGAM1447 is therefore inhibition of FLJ13614 (Accession NM_139076). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13614. FLJ13881 (Accession NM_024729) is another VGAM1447 host target gene. FLJ13881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13881 BINDING SITE, designated SEQ ID:24067, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50310] Another function of VGAM1447 is therefore inhibition of FLJ13881 (Accession NM_024729). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ13881. FLJ14082 (Accession NM_025024) is another VGAM1447 host target gene. FLJ14082 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14082 BINDING SITE, designated SEQ ID:24609, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50311] Another function of VGAM1447 is therefore inhibition of FLJ14082 (Accession NM_025024). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14082. FLJ14117 (Accession NM_022777) is another VGAM1447 host target gene. FLJ14117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14117 BINDING SITE, designated SEQ ID:23049, to the nucleotide

sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50312] Another function of VGAM1447 is therefore inhibition of FLJ14117 (Accession NM_022777). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14117. FLJ21106 (Accession NM_025097) is another VGAM1447 host target gene. FLJ21106 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ21106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21106 BINDING SITE, designated SEQ ID:24734, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50313] Another function of VGAM1447 is therefore inhibition of FLJ21106 (Accession NM_025097). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21106. FLJ32389 (Accession NM_144617) is another VGAM1447 host target gene. FLJ32389 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ32389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32389 BINDING SITE, designated SEQ ID:29435, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50314] Another function of VGAM1447 is therefore inhibition of FLJ32389 (Accession NM_144617). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32389. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12 (GalNAc-T12) (GALNT12, Accession NM_024642) is another VGAM1447 host target gene. GALNT12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT12 BINDING SITE, designated SEQ ID:23927, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4158.

[50315] Another function of VGAM1447 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12 (GalNAc-T12) (GALNT12, Accession NM_024642). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT12. HPIP (Accession NM_020524) is another VGAM1447 host target gene. HPIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPIP BINDING SITE, designated SEQ ID:21736, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50316] Another function of VGAM1447 is therefore inhibition of HPIP (Accession NM_020524). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPIP. HRIHFB2122 (Accession NM_007032) is another VGAM1447 host target gene. HRIHFB2122 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRIHFB2122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRIHFB2122 BINDING SITE, designated SEQ ID:13899, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50317] Another function of VGAM1447 is therefore inhibition of HRIHFB2122 (Accession NM_007032). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRIHFB2122. KIAA0057 (Accession NM_012288) is another VGAM1447 host target gene. KIAA0057 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0057 BINDING SITE, designated SEQ ID:14626, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50318] Another function of VGAM1447 is therefore inhibition of

KIAA0057 (Accession NM_012288). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0057. KIAA0194 (Accession XM_038362) is another VGAM1447 host target gene. KIAA0194 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0194 BINDING SITE, designated SEQ ID:32823, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50319] Another function of VGAM1447 is therefore inhibition of KIAA0194 (Accession XM_038362). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0194. KIAA0444 (Accession XM_030999) is another VGAM1447 host target gene. KIAA0444 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0444, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0444 BINDING SITE, designated SEQ ID:31246, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50320] Another function of VGAM1447 is therefore inhibition of KIAA0444 (Accession XM_030999). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0444. KIAA0470 (Accession NM_014812) is another VGAM1447 host target gene. KIAA0470 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0470 BINDING SITE, designated SEQ ID:16777, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50321] Another function of VGAM1447 is therefore inhibition of KIAA0470 (Accession NM_014812). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0470. KIAA0663 (Accession NM_014827) is another

VGAM1447 host target gene. KIAA0663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0663 BINDING SITE, designated SEQ ID:16815, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50322] Another function of VGAM1447 is therefore inhibition of KIAA0663 (Accession NM_014827). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0663. KIAA1155 (Accession XM_030864) is another VGAM1447 host target gene. KIAA1155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1155 BINDING SITE, designated SEQ ID:31200, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50323] Another function of VGAM1447 is therefore inhibition of KIAA1155 (Accession XM_030864). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1155. KIAA1416 (Accession XM_098762) is another VGAM1447 host target gene. KIAA1416 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1416 BINDING SITE, designated SEQ ID:41803, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50324] Another function of VGAM1447 is therefore inhibition of KIAA1416 (Accession XM_098762). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1416. KIAA1656 (Accession XM_038022) is another VGAM1447 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32729, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50325] Another function of VGAM1447 is therefore inhibition of KIAA1656 (Accession XM_038022). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1656. MGC20253 (Accession NM_144583) is another VGAM1447 host target gene. MGC20253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20253 BINDING SITE, designated SEQ ID:29398, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50326] Another function of VGAM1447 is therefore inhibition of MGC20253 (Accession NM_144583). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC20253. MGC4655 (Accession NM_033309) is another VGAM1447 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655 BINDING SITE, designated SEQ ID:27149, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50327] Another function of VGAM1447 is therefore inhibition of MGC4655 (Accession NM_033309). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564) is another VGAM1447 host target gene. SLC39A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC39A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC39A3 BINDING SITE, designated SEQ ID:29358, to the nucleotide

sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50328] Another function of VGAM1447 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC39A3. Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM_004782) is another VGAM1447 host target gene. SNAP29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNAP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNAP29 BINDING SITE, designated SEQ ID:11186, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50329] Another function of VGAM1447 is therefore inhibition of Synaptosomal-associated Protein, 29kDa (SNAP29, Accession NM_004782). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNAP29. Serum Re-

sponse Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131) is another VGAM1447 host target gene. SRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRF BINDING SITE, designated SEQ ID:9105, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50330] Another function of VGAM1447 is therefore inhibition of Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRF. Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202) is another VGAM1447 host target gene. SS18L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SS18L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SS18L1 BINDING SITE, designated SEQ ID:32561, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50331] Another function of VGAM1447 is therefore inhibition of Synovial Sarcoma Translocation Gene On Chromosome 18-like 1 (SS18L1, Accession XM_037202). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18L1. SYNE-1 (Accession NM_015293) is another VGAM1447 host target gene. SYNE-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNE-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNE-1 BINDING SITE, designated SEQ ID:17614, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50332] Another function of VGAM1447 is therefore inhibition of SYNE-1 (Accession NM_015293). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with SYNE-1. TED (Accession NM_015686) is another VGAM1447 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17913, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50333] Another function of VGAM1447 is therefore inhibition of TED (Accession NM_015686). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED. Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM_080872) is another VGAM1447 host target gene. UNC5D BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UNC5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC5D BINDING SITE, designated SEQ

ID:28115, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50334] Another function of VGAM1447 is therefore inhibition of Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM_080872). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5D. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023) is another VGAM1447 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27579, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50335] Another function of VGAM1447 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. LOC116437

(Accession XM_058185) is another VGAM1447 host target gene. LOC116437 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC116437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116437 BINDING SITE, designated SEQ ID:36579, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50336] Another function of VGAM1447 is therefore inhibition of LOC116437 (Accession XM_058185). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116437. LOC118987 (Accession XM_058361) is another VGAM1447 host target gene. LOC118987 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC118987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118987 BINDING SITE, designated SEQ ID:36608, to the nucleotide sequence of VGAM1447 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4158.

[50337] Another function of VGAM1447 is therefore inhibition of LOC118987 (Accession XM_058361). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118987. LOC121219 (Accession XM_058544) is another VGAM1447 host target gene. LOC121219 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC121219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121219 BINDING SITE, designated SEQ ID:36652, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50338] Another function of VGAM1447 is therefore inhibition of LOC121219 (Accession XM_058544). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121219. LOC121506 (Accession XM_058570) is another VGAM1447 host target gene. LOC121506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121506, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121506 BINDING SITE, designated SEQ ID:36668, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50339] Another function of VGAM1447 is therefore inhibition of LOC121506 (Accession XM_058570). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121506. LOC145225 (Accession XM_096741) is another VGAM1447 host target gene. LOC145225 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145225 BINDING SITE, designated SEQ ID:40524, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50340] Another function of VGAM1447 is therefore inhibition of LOC145225 (Accession XM_096741). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC145225. LOC150054 (Accession XM_097797) is another VGAM1447 host target gene. LOC150054 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150054 BINDING SITE, designated SEQ ID:41125, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50341] Another function of VGAM1447 is therefore inhibition of LOC150054 (Accession XM_097797). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150054. LOC151521 (Accession XM_098076) is another VGAM1447 host target gene. LOC151521 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC151521, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151521 BINDING SITE, designated SEQ ID:41368, to

the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50342] Another function of VGAM1447 is therefore inhibition of LOC151521 (Accession XM_098076). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151521. LOC219673 (Accession XM_167567) is another VGAM1447 host target gene. LOC219673 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219673, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219673 BINDING SITE, designated SEQ ID:44694, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50343] Another function of VGAM1447 is therefore inhibition of LOC219673 (Accession XM_167567). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219673. LOC220766 (Accession XM_165471) is another VGAM1447 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43656, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50344] Another function of VGAM1447 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC253350 (Accession XM_174261) is another VGAM1447 host target gene. LOC253350 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253350 BINDING SITE, designated SEQ ID:46586, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50345] Another function of VGAM1447 is therefore inhibition of LOC253350 (Accession XM_174261). Accordingly, utilities

of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253350. LOC257336 (Accession XM_171216) is another VGAM1447 host target gene. LOC257336 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257336 BINDING SITE, designated SEQ ID:46002, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50346] Another function of VGAM1447 is therefore inhibition of LOC257336 (Accession XM_171216). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257336. LOC257358 (Accession XM_173138) is another VGAM1447 host target gene. LOC257358 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC257358 BINDING SITE, designated SEQ ID:46390, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50347] Another function of VGAM1447 is therefore inhibition of LOC257358 (Accession XM_173138). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257358. LOC51634 (Accession NM_016024) is another VGAM1447 host target gene. LOC51634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51634 BINDING SITE, designated SEQ ID:18102, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50348] Another function of VGAM1447 is therefore inhibition of LOC51634 (Accession NM_016024). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51634. LOC91133 (Accession XM_036372) is another VGAM1447 host target gene. LOC91133 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91133 BINDING SITE, designated SEQ ID:32430, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50349] Another function of VGAM1447 is therefore inhibition of LOC91133 (Accession XM_036372). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91133. LOC92344 (Accession XM_044455) is another VGAM1447 host target gene. LOC92344 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92344, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92344 BINDING SITE, designated SEQ ID:34209, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50350] Another function of VGAM1447 is therefore inhibition of

LOC92344 (Accession XM_044455). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92344. LOC93070 (Accession XM_049046) is another VGAM1447 host target gene. LOC93070 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93070 BINDING SITE, designated SEQ ID:35326, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50351] Another function of VGAM1447 is therefore inhibition of LOC93070 (Accession XM_049046). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93070. LOC93259 (Accession XM_050105) is another VGAM1447 host target gene. LOC93259 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC93259 BINDING SITE, designated SEQ ID:35561, to the nucleotide sequence of VGAM1447 RNA, herein designated VGAM RNA, also designated SEQ ID:4158.

[50352] Another function of VGAM1447 is therefore inhibition of LOC93259 (Accession XM_050105). Accordingly, utilities of VGAM1447 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93259. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1448 (VGAM1448) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50353] VGAM1448 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1448 was detected is described hereinabove with reference to Figs. 1–8.

[50354] VGAM1448 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pepper Mottle Virus. VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[50355] VGAM1448 gene encodes a VGAM1448 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1448 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1448 precursor RNA is designated SEQ ID:1434, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1434 is located at position 8114 relative to the genome of Pepper Mottle Virus.

[50356] VGAM1448 precursor RNA folds onto itself, forming VGAM1448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50357] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1448 folded precursor RNA into VGAM1448 RNA, herein designated VGAM RNA, a single stranded ~22

nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1448 RNA is designated SEQ ID:4159, and is provided hereinbelow with reference to the sequence listing part.

[50358] VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1448 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50359] VGAM1448 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1448 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1448 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50360] The complementary binding of VGAM1448 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1448 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1448 host target RNA into VGAM1448 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50361] It is appreciated that VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1448 host target genes. The mRNA of each one of this plurality of VGAM1448 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1448 RNA, herein designated VGAM RNA, and which when bound by VGAM1448 RNA causes inhibition of translation of respective one or more VGAM1448 host target proteins.

[50362] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1448 gene, herein designated VGAM GENE, on one or more VGAM1448 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50363] It is yet further appreciated that a function of VGAM1448 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGAM1448 correlate with, and may be deduced from, the identity of the host target genes which VGAM1448 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50364] Nucleotide sequences of the VGAM1448 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1448 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1448 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1448 are further described hereinbelow with reference to Table 1.

[50365] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM1448 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1448 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50366] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1448 gene, herein designated VGAM is inhibition of expression of VGAM1448 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1448 correlate with, and may be deduced from, the identity of the target genes which VGAM1448 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50367] M-phase Phosphoprotein 9 (MPHOSPH9, Accession NM_022782) is a VGAM1448 host target gene. MPHOSPH9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPHOSPH9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPHOSPH9 BINDING SITE, designated SEQ ID:23065, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ

ID:4159.

[50368] A function of VGAM1448 is therefore inhibition of M-phase Phosphoprotein 9 (MPHOSPH9, Accession NM_022782). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPHOSPH9. DKFZP566J2046 (Accession NM_031208) is another VGAM1448 host target gene. DKFZP566J2046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566J2046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566J2046 BINDING SITE, designated SEQ ID:25251, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ ID:4159.

[50369] Another function of VGAM1448 is therefore inhibition of DKFZP566J2046 (Accession NM_031208). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566J2046. NY-REN-60 (Accession XM_040506) is another VGAM1448 host target gene. NY-REN-60 BIND-

ING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-60, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-60 BINDING SITE, designated SEQ ID:33317, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ ID:4159.

[50370] Another function of VGAM1448 is therefore inhibition of NY-REN-60 (Accession XM_040506). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-60. Zinc Finger, DHHC Domain Containing 5 (ZDHHC5, Accession XM_166204) is another VGAM1448 host target gene. ZDHHC5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZDHHC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC5 BINDING SITE, designated SEQ ID:44009, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ ID:4159.

[50371] Another function of VGAM1448 is therefore inhibition of Zinc Finger, DHHC Domain Containing 5 (ZDHHC5, Accession XM_166204). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC5. LOC196549 (Accession NM_145293) is another VGAM1448 host target gene. LOC196549 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196549 BINDING SITE, designated SEQ ID:29808, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ ID:4159.

[50372] Another function of VGAM1448 is therefore inhibition of LOC196549 (Accession NM_145293). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196549. LOC205327 (Accession XM_115788) is another VGAM1448 host target gene. LOC205327 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC205327, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205327 BINDING SITE, designated SEQ ID:43104, to the nucleotide sequence of VGAM1448 RNA, herein designated VGAM RNA, also designated SEQ ID:4159.

[50373] Another function of VGAM1448 is therefore inhibition of LOC205327 (Accession XM_115788). Accordingly, utilities of VGAM1448 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205327. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1449 (VGAM1449) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50374] VGAM1449 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1449 was detected is described hereinabove with reference to Figs. 1-8.

[50375] VGAM1449 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2.

VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50376] VGAM1449 gene encodes a VGAM1449 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1449 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1449 precursor RNA is designated SEQ ID:1435, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1435 is located at position 38531 relative to the genome of Equine Herpesvirus 2.

[50377] VGAM1449 precursor RNA folds onto itself, forming VGAM1449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50378] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1449 folded precursor RNA into VGAM1449 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 92%) nucleotide sequence of VGAM1449 RNA is designated SEQ ID:4160, and is provided hereinbelow with reference to the sequence listing part.

[50379] VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1449 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50380] VGAM1449 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1449 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1449 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50381] The complementary binding of VGAM1449 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1449 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1449 host target RNA into VGAM1449 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50382] It is appreciated that VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1449 host target genes. The mRNA of each one of this plurality of VGAM1449 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1449 RNA, herein designated VGAM RNA, and which when bound by VGAM1449 RNA causes inhibition of translation of respective one or more VGAM1449 host target proteins.

[50383] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1449 gene, herein designated VGAM GENE, on one or more VGAM1449 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50384] It is yet further appreciated that a function of VGAM1449 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1449 correlate with, and may be deduced from, the identity of the host target genes which VGAM1449 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50385] Nucleotide sequences of the VGAM1449 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1449 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1449 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1449 are further described hereinbelow with reference to Table 1.

[50386] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1449 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1449 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50387] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1449 gene, herein designated VGAM is inhibition of expression of VGAM1449 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1449 correlate with, and may be deduced from, the identity of the target genes which VGAM1449 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50388] ALEX2 (Accession NM_014782) is a VGAM1449 host target gene. ALEX2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ALEX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALEX2 BINDING SITE, designated SEQ ID:16634, to the nucleotide sequence of VGAM1449 RNA,

herein designated VGAM RNA, also designated SEQ ID:4160.

[50389] A function of VGAM1449 is therefore inhibition of ALEX2 (Accession NM_014782), a gene which play a role in tumor suppression, possibly by being involved in the regulation of normal cell growth. Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALEX2. The function of ALEX2 has been established by previous studies. Armadillo (arm) repeat proteins (e.g., beta-catenin; 116806), are involved in development, maintenance of tissue integrity, and tumorigenesis. Their common feature is a 42-amino acid motif, the arm repeat. Using a yeast 2-hybrid screen of a brain cDNA library to identify proteins interacting with the peroxisome protease PP110, Kurochkin et al. (2001) identified a cDNA encoding ALEX1. They also cloned a cDNA encoding ALEX1 by screening a testis cDNA library. By searching sequence databases for homologs of ALEX1, they identified cDNAs encoding ALEX2 (OMIM Ref. No. 300363) and ALEX3 (OMIM Ref. No. 300364). Sequence analysis predicted that the 453-amino acid ALEX1 protein contains a potential N-terminal trans-membrane domain, 2 arm repeats, an ATP/GTP-binding

site, and multiple phosphorylation sites. Northern blot and RT-PCR analyses revealed wide expression of a 2.2-kb ALEX1 transcript in normal tissues and cancer cell lines; no expression was detected in carcinomas.

Kurochkin et al. (2001) proposed that the specific loss of expression in epithelial tissue tumors suggests that the ALEX proteins play a role in tumor suppression, possibly by being involved in the regulation of normal cell growth.

[50390] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50391] Kurochkin, I. V.; Yonemitsu, N.; Funahashi, S.; Nomura, H. : ALEX1, a novel human armadillo repeat protein that is expressed differentially in normal tissues and carcinomas. Biochem. Biophys. Res. Commun. 280: 340–347, 2001. ; and

[50392] CREATION DATE.

[50393] Further studies establishing the function and utilities of ALEX2 are found in John Hopkins OMIM database record ID 300363, and in cited publications numbered 6734–6735 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Forkhead Box E1 (thyroid transcription factor 2) (FOXE1, Accession

NM_004473) is another VGAM1449 host target gene.

FOX E1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FOX E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOX E1 BINDING SITE, designated SEQ ID:10780, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50394] Another function of VGAM1449 is therefore inhibition of Forkhead Box E1 (thyroid transcription factor 2) (FOX E1, Accession NM_004473). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOX E1. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM1449 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32201,

to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50395] Another function of VGAM1449 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Sorting Nexin 5 (SNX5, Accession NM_014426) is another VGAM1449 host target gene. SNX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX5 BINDING SITE, designated SEQ ID:15785, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50396] Another function of VGAM1449 is therefore inhibition of Sorting Nexin 5 (SNX5, Accession NM_014426). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX5. Transcription Factor Dp-1 (TFDP1, Accession NM_007111) is another VGAM1449 host target gene.

TFDP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFDP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFDP1 BINDING SITE, designated SEQ ID:13976, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50397] Another function of VGAM1449 is therefore inhibition of Transcription Factor Dp-1 (TFDP1, Accession NM_007111). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFDP1. Chromosome 5 Open Reading Frame 5 (C5orf5, Accession NM_016603) is another VGAM1449 host target gene. C5orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf5 BINDING SITE, designated SEQ ID:18698, to the nucleotide sequence of VGAM1449 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4160.

[50398] Another function of VGAM1449 is therefore inhibition of Chromosome 5 Open Reading Frame 5 (C5orf5, Accession NM_016603). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf5. FLJ20552 (Accession NM_017876) is another VGAM1449 host target gene. FLJ20552 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20552, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20552 BINDING SITE, designated SEQ ID:19548, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50399] Another function of VGAM1449 is therefore inhibition of FLJ20552 (Accession NM_017876). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20552. P114-RHO-GEF (Accession NM_015318) is another VGAM1449 host target gene. P114-RHO-GEF BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by P114-RHO-GEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P114-RHO-GEF BINDING SITE, designated SEQ ID:17640, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50400] Another function of VGAM1449 is therefore inhibition of P114-RHO-GEF (Accession NM_015318). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P114-RHO-GEF. LOC118851 (Accession XM_061180) is another VGAM1449 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, designated SEQ ID:37201, to the nucleotide sequence of VGAM1449 RNA, herein designated VGAM RNA, also designated SEQ ID:4160.

[50401] Another function of VGAM1449 is therefore inhibition of LOC118851 (Accession XM_061180). Accordingly, utilities of VGAM1449 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118851. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1450 (VGAM1450) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50402] VGAM1450 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1450 was detected is described hereinabove with reference to Figs. 1–8.

[50403] VGAM1450 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50404] VGAM1450 gene encodes a VGAM1450 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1450 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1450 precursor RNA is designated SEQ ID:1436, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1436 is located at position 40972 relative to the genome of Equine Herpesvirus 2.

- [50405] VGAM1450 precursor RNA folds onto itself, forming VGAM1450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [50406] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1450 folded precursor RNA into VGAM1450 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1450 RNA is designated SEQ ID:4161, and is provided hereinbelow with reference to the sequence listing part.

[50407] VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1450 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50408] VGAM1450 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1450 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1450 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50409] The complementary binding of VGAM1450 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1450 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1450 host target RNA into VGAM1450 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50410] It is appreciated that VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1450 host target genes. The mRNA of each one of this plurality of VGAM1450 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1450 RNA, herein designated VGAM RNA, and which when bound by VGAM1450 RNA causes inhibition of translation of respective one or more VGAM1450 host target proteins.

[50411] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1450 gene, herein designated VGAM GENE, on one or more VGAM1450 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50412] It is yet further appreciated that a function of VGAM1450 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1450 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1450 correlate with, and may be deduced from, the identity of the host target genes which VGAM1450 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50413] Nucleotide sequences of the VGAM1450 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1450 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1450 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1450 are further described hereinbelow with reference to Table 1.

[50414] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1450 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1450 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[50415] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1450 gene, herein designated VGAM is inhibition of expression of VGAM1450 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1450 correlate with, and may be deduced from, the identity of the target genes which VGAM1450 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50416] KIAA1128 (Accession XM_043596) is a VGAM1450 host target gene. KIAA1128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1128 BINDING SITE, designated SEQ ID:33969, to the nucleotide sequence of VGAM1450 RNA, herein designated VGAM RNA, also designated SEQ ID:4161.

[50417] A function of VGAM1450 is therefore inhibition of KIAA1128 (Accession XM_043596). Accordingly, utilities of VGAM1450 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1128. LOC150225 (Accession XM_097870) is another VGAM1450 host target gene. LOC150225 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150225, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150225 BINDING SITE, designated SEQ ID:41184, to the nucleotide sequence of VGAM1450 RNA, herein designated VGAM RNA, also designated SEQ ID:4161.

[50418] Another function of VGAM1450 is therefore inhibition of LOC150225 (Accession XM_097870). Accordingly, utilities of VGAM1450 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150225. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1451 (VGAM1451) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50419] VGAM1451 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1451 was detected is described hereinabove with reference to Figs. 1–8.

[50420] VGAM1451 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50421] VGAM1451 gene encodes a VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1451 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1451 precursor RNA is designated SEQ ID:1437, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1437 is located at position 40488 relative to the genome of Equine Herpesvirus 2.

[50422] VGAM1451 precursor RNA folds onto itself, forming VGAM1451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50423] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1451 folded precursor RNA into VGAM1451 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1451 RNA is designated SEQ ID:4162, and is provided hereinbelow with reference to the sequence listing part.

[50424] VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1451 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50425] VGAM1451 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1451 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1451 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[50426] The complementary binding of VGAM1451 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1451 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1451 host target RNA into VGAM1451 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50427] It is appreciated that VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1451 host target genes. The mRNA of each one of this plurality of VGAM1451 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1451 RNA, herein designated VGAM RNA, and which when bound by VGAM1451 RNA causes inhibition of translation of respective one or more VGAM1451 host target proteins.

[50428] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1451 gene, herein designated VGAM GENE, on one or more VGAM1451 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50429] It is yet further appreciated that a function of VGAM1451 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1451 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1451 correlate with, and may be deduced from, the identity of the host target genes which VGAM1451 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50430] Nucleotide sequences of the VGAM1451 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1451 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1451 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1451 are further described hereinbelow with reference to Table 1.

[50431] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1451 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1451 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50432] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1451 gene, herein designated VGAM is inhibition of expression of VGAM1451 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1451 correlate with, and may be deduced from, the identity of the target genes which VGAM1451 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50433] Cyclin T2 (CCNT2, Accession NM_058241) is a VGAM1451 host target gene. CCNT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNT2, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNT2 BINDING SITE, designated SEQ ID:27769, to the nucleotide sequence of VGAM1451 RNA, herein designated VGAM RNA, also designated SEQ ID:4162.

[50434] A function of VGAM1451 is therefore inhibition of Cyclin T2 (CCNT2, Accession NM_058241), a gene which is a regulatory subunit of the cyclin-dependent kinase pair (cdk9/cyclin t) complex. Accordingly, utilities of VGAM1451 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNT2. The function of CCNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM159. KIAA1161 (Accession XM_088501) is another VGAM1451 host target gene. KIAA1161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1161 BINDING SITE, designated SEQ ID:39744, to the

nucleotide sequence of VGAM1451 RNA, herein designated VGAM RNA, also designated SEQ ID:4162.

[50435] Another function of VGAM1451 is therefore inhibition of KIAA1161 (Accession XM_088501). Accordingly, utilities of VGAM1451 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1161. KIAA1274 (Accession XM_166125) is another VGAM1451 host target gene. KIAA1274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1274 BINDING SITE, designated SEQ ID:43907, to the nucleotide sequence of VGAM1451 RNA, herein designated VGAM RNA, also designated SEQ ID:4162.

[50436] Another function of VGAM1451 is therefore inhibition of KIAA1274 (Accession XM_166125). Accordingly, utilities of VGAM1451 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1274. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 1452 (VGAM1452) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50437] VGAM1452 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1452 was detected is described hereinabove with reference to Figs. 1–8.

[50438] VGAM1452 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50439] VGAM1452 gene encodes a VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1452 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1452 precursor RNA is designated SEQ ID:1438, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1438 is located at position 42439 relative to the genome of Equine Herpesvirus 2.

[50440] VGAM1452 precursor RNA folds onto itself, forming VGAM1452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50441] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1452 folded precursor RNA into VGAM1452 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1452 RNA is designated SEQ ID:4163, and is provided hereinbelow with reference to the sequence listing part.

[50442] VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1452 host target RNA, herein designated

VGAM HOST TARGET RNA. VGAM1452 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50443] VGAM1452 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1452 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1452 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50444] The complementary binding of VGAM1452 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1452 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1452 host target RNA into VGAM1452 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50445] It is appreciated that VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1452 host target genes. The mRNA of each one of this plurality of VGAM1452 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1452 RNA, herein designated VGAM RNA, and which when bound by VGAM1452 RNA causes inhibition of translation of respective one or more VGAM1452 host target proteins.

[50446] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1452 gene, herein designated VGAM GENE, on one or more VGAM1452 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50447] It is yet further appreciated that a function of VGAM1452 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1452 correlate with, and may be deduced from, the identity of

the host target genes which VGAM1452 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50448] Nucleotide sequences of the VGAM1452 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1452 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1452 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1452 are further described hereinbelow with reference to Table 1.

[50449] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1452 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1452 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50450] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1452 gene, herein designated VGAM is inhibition of expression of VGAM1452 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1452 correlate with, and may be deduced from, the identity of the target genes which VGAM1452

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50451] Cytoplasmic FMR1 Interacting Protein 2 (CYFIP2, Accession XM_056963) is a VGAM1452 host target gene. CYFIP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CYFIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYFIP2 BINDING SITE, designated SEQ ID:36440, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50452] A function of VGAM1452 is therefore inhibition of Cytoplasmic FMR1 Interacting Protein 2 (CYFIP2, Accession XM_056963). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYFIP2. ELL (Accession NM_006532) is another VGAM1452 host target gene. ELL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

ELL BINDING SITE, designated SEQ ID:13279, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50453] Another function of VGAM1452 is therefore inhibition of ELL (Accession NM_006532). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELL. GNAS Complex Locus (GNAS, Accession NM_016592) is another VGAM1452 host target gene. GNAS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNAS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAS BINDING SITE, designated SEQ ID:18680, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50454] Another function of VGAM1452 is therefore inhibition of GNAS Complex Locus (GNAS, Accession NM_016592), a gene which transduces signals from G protein-coupled receptors and activates adenylyl cyclase. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with GNAS. The function of GNAS and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1205. Growth Factor Receptor-bound Protein 10 (GRB10, Accession NM_005311) is another VGAM1452 host target gene. GRB10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GRB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRB10 BINDING SITE, designated SEQ ID:11784, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50455] Another function of VGAM1452 is therefore inhibition of Growth Factor Receptor-bound Protein 10 (GRB10, Accession NM_005311), a gene which plays a functional role in insulin and IGF-I signaling. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRB10. The function of GRB10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM441.SET Binding Factor 1 (SBF1, Accession XM_037447) is another VGAM1452 host target gene. SBF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SBF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBF1 BINDING SITE, designated SEQ ID:32625, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50456] Another function of VGAM1452 is therefore inhibition of SET Binding Factor 1 (SBF1, Accession XM_037447), a gene which is of unknown function, could be a tyrosine-phosphatase. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBF1. The function of SBF1 has been established by previous studies. Mutations in the myotubularin (MTM1; 310400) dual-specific phosphatase (DSP) gene cause X-linked myotubular myopathy. By searching an EST database for sequences related to MTM1, Laporte et al. (1998) identified a partial MTMR5 (myotubularin-related protein-5) cDNA and cDNAs encoding 3 other novel members of the myotubularin (MTM)

protein family. They noted that the predicted protein lacks catalytically essential residues in the tyrosine phosphatase/DSP active site. Northern blot analysis revealed that the 6-kb MTMR5 mRNA was expressed in all tissues tested but testis. The SET (Suvar3-9, Enhancer of zeste, trithorax) domain was originally identified as a characteristic motif in several *Drosophila* proteins that contribute to epigenetic mechanisms of gene regulation. The human protooncoprotein HRX (OMIM Ref. No. 159555) also contains a SET domain. Using a yeast 2-hybrid assay with the SET domain of HRX as bait, Cui et al. (1998) isolated cDNAs encoding MTMR5, or SBF1 (SET-binding factor 1). Both SBF1 and MTM1 interacted with HRX in vitro and in vivo. This interaction was abrogated in an oncogenic form of HRX lacking the SET domain. Like HRX, both SBF1 and MTM1 localized to the nucleus of mammalian cells. The authors found that the SET interaction domain (SID) of the SBF1 protein displays a paired amphipathic helix secondary structure. The SID is highly conserved in the myotubularin-related family of proteins. In contrast with MTM1, SBF1 lacked dual-specificity phosphatase activity in vitro, suggesting that SBF1 acts as a protective factor that prevents substrate dephosphorylation. Ectopic ex-

pression of SBF1 induced NIH 3T3 cell transformation, leading Cui et al. (1998) to propose that displacement or exclusion of endogenous, catalytically active phosphatases from SET-domain proteins is a critical molecular event underlying loss of growth control. Similarly, ectopic expression of SBF1 impaired the in vitro differentiation of myoblast cells, implying that interactions of SET-domain proteins with catalytically active members of the MTM family are essential for execution of the myogenic program. The authors concluded that MTM-type phosphatases link SET domain-containing components of the epigenetic regulatory machinery with signaling pathways involved in growth and differentiation.

[50457] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50458] Cui, X.; De Vivo, I.; Slany, R.; Miyamoto, A.; Firestein, R.; Cleary, M. L. : Association of SET domain and myotubularin-related proteins modulates growth control. *Nature Genet.* 18: 331–337, 1998. ; and

[50459] Laporte, J.; Blondeau, F.; Buj-Bello, A.; Tentler, D.; Kretz, C.; Dahl, N.; Mandel, J.-L. : Characterization of the myotubularin dual specificity phosphatase gene family from

yeast to h.

[50460] Further studies establishing the function and utilities of SBF1 are found in John Hopkins OMIM database record ID 603560, and in cited publications numbered 500 and 7254 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite Motif-containing 14 (TRIM14, Accession NM_014788) is another VGAM1452 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM14 BINDING SITE, designated SEQ ID:16665, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50461] Another function of VGAM1452 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM_014788), a gene which is composed of 3 zinc-binding domains and is involved in development and cell growth. Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 and

its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM180.Chromosome 11 Open Reading Frame 9

(C11orf9, Accession NM_013279) is another VGAM1452 host target gene. C11orf9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C11orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf9 BINDING SITE, designated SEQ ID:14947, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50462] Another function of VGAM1452 is therefore inhibition of Chromosome 11 Open Reading Frame 9 (C11orf9, Accession NM_013279). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf9. Chromosome 5 Open Reading Frame 7 (C5orf7, Accession XM_033576) is another VGAM1452 host target gene. C5orf7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C5orf7, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf7 BINDING SITE, designated SEQ ID:31940, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50463] Another function of VGAM1452 is therefore inhibition of Chromosome 5 Open Reading Frame 7 (C5orf7, Accession XM_033576). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf7. CXYorf1 (Accession XM_088704) is another VGAM1452 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39911, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50464] Another function of VGAM1452 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of

VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXY-orf1. FLJ10743 (Accession NM_018201) is another VGAM1452 host target gene. FLJ10743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10743 BINDING SITE, designated SEQ ID:20080, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50465] Another function of VGAM1452 is therefore inhibition of FLJ10743 (Accession NM_018201). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10743. FLJ22593 (Accession NM_024703) is another VGAM1452 host target gene. FLJ22593 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22593, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22593

BINDING SITE, designated SEQ ID:24017, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50466] Another function of VGAM1452 is therefore inhibition of FLJ22593 (Accession NM_024703). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22593. FLJ22944 (Accession NM_025145) is another VGAM1452 host target gene. FLJ22944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22944 BINDING SITE, designated SEQ ID:24782, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50467] Another function of VGAM1452 is therefore inhibition of FLJ22944 (Accession NM_025145). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22944. KIAA0620 (Accession XM_030707) is another VGAM1452 host target gene. KIAA0620 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0620 BINDING SITE, designated SEQ ID:31119, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50468] Another function of VGAM1452 is therefore inhibition of KIAA0620 (Accession XM_030707). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0620. KIAA0864 (Accession XM_032630) is another VGAM1452 host target gene. KIAA0864 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0864, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0864 BINDING SITE, designated SEQ ID:31683, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50469] Another function of VGAM1452 is therefore inhibition of

KIAA0864 (Accession XM_032630). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0864. KIAA1432 (Accession XM_039698) is another VGAM1452 host target gene. KIAA1432 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1432 BINDING SITE, designated SEQ ID:33151, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50470] Another function of VGAM1452 is therefore inhibition of KIAA1432 (Accession XM_039698). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. KIAA1719 (Accession XM_042936) is another VGAM1452 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33822, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50471] Another function of VGAM1452 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. LOC129607 (Accession XM_059368) is another VGAM1452 host target gene. LOC129607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129607 BINDING SITE, designated SEQ ID:36974, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50472] Another function of VGAM1452 is therefore inhibition of LOC129607 (Accession XM_059368). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129607. LOC154089 (Accession XM_087846) is an-

other VGAM1452 host target gene. LOC154089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154089 BINDING SITE, designated SEQ ID:39463, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50473] Another function of VGAM1452 is therefore inhibition of LOC154089 (Accession XM_087846). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154089. LOC200093 (Accession XM_032184) is another VGAM1452 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31603, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50474] Another function of VGAM1452 is therefore inhibition of LOC200093 (Accession XM_032184). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC221876 (Accession XM_168220) is another VGAM1452 host target gene. LOC221876 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC221876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221876 BINDING SITE, designated SEQ ID:45076, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50475] Another function of VGAM1452 is therefore inhibition of LOC221876 (Accession XM_168220). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221876. LOC91040 (Accession XM_035641) is another VGAM1452 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32320, to the nucleotide sequence of VGAM1452 RNA, herein designated VGAM RNA, also designated SEQ ID:4163.

[50476] Another function of VGAM1452 is therefore inhibition of LOC91040 (Accession XM_035641). Accordingly, utilities of VGAM1452 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1453 (VGAM1453) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50477] VGAM1453 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1453 was detected is described hereinabove with reference to Figs. 1–8.

[50478] VGAM1453 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1453 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[50479] VGAM1453 gene encodes a VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1453 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1453 precursor RNA is designated SEQ ID:1439, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1439 is located at position 41504 relative to the genome of Equine Herpesvirus 2.

[50480] VGAM1453 precursor RNA folds onto itself, forming VGAM1453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50481] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1453 folded precursor RNA into VGAM1453

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1453 RNA is designated SEQ ID:4164, and is provided hereinbelow with reference to the sequence listing part.

[50482] VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1453 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50483] VGAM1453 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1453 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1453 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50484] The complementary binding of VGAM1453 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1453 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1453 host target RNA into VGAM1453 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[50485] It is appreciated that VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1453 host target genes. The mRNA of each one of this plurality of VGAM1453 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1453 RNA, herein designated VGAM RNA, and which when bound by VGAM1453 RNA causes inhibition of translation of respective one or more VGAM1453 host target proteins.

[50486] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1453 gene, herein designated VGAM GENE, on one or more VGAM1453 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50487] It is yet further appreciated that a function of VGAM1453 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1453 correlate with, and may be deduced from, the identity of the host target genes which VGAM1453 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50488] Nucleotide sequences of the VGAM1453 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1453 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1453 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1453 are further described hereinbelow with reference to Table 1.

[50489] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1453 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1453 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50490] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1453 gene, herein designated VGAM is inhibition of expression of VGAM1453 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1453 correlate with, and may be deduced from, the identity of the target genes which VGAM1453 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50491] CERD4 (Accession NM_012074) is a VGAM1453 host target gene. CERD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CERD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CERD4 BINDING SITE, designated SEQ ID:14341, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ

ID:4164.

[50492] A function of VGAM1453 is therefore inhibition of CERD4 (Accession NM_012074). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CERD4. Chorea Acanthocytosis (CHAC, Accession NM_033305) is another VGAM1453 host target gene. CHAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHAC BINDING SITE, designated SEQ ID:27139, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50493] Another function of VGAM1453 is therefore inhibition of Chorea Acanthocytosis (CHAC, Accession NM_033305), a gene which may regulate the cycling of proteins. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHAC. The function of CHAC and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM650. Corticotropin Releasing Hormone (CRH, Accession NM_000756) is another VGAM1453 host target gene. CRH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CRH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRH BINDING SITE, designated SEQ ID:6409, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50494] Another function of VGAM1453 is therefore inhibition of Corticotropin Releasing Hormone (CRH, Accession NM_000756), a gene which regulates the release of corticotropin from pituitary gland. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRH. The function of CRH has been established by previous studies. Response to stress in mammals requires an intact hypothalamic-pituitary-adrenal axis. The proximal part of the response is mediated by secretion of corticotropin-releasing hormone (CRH) by the paraventricular nucleus of the hypothalamus. CRH is a 41-amino acid peptide derived by

enzymatic cleavage from a 191-amino acid preprohormone. Shibahara et al. (1983) cloned and sequenced the human CRH gene. Arbiser et al. (1988) assigned the gene for CRH to 8q13 by somatic cell hybrid and in situ hybridization studies. The absence of secondary hybridization strongly suggested that hypothalamic and placental CRH are transcribed from the same gene. Kellogg et al. (1989) corroborated the assignment to 8q13 by in situ hybridization. Knapp et al. (1993) showed that the homologous gene is located on mouse chromosome 3. Sebaceous glands may be involved in a pathway conceptually similar to that of the hypothalamic-pituitary-adrenal (HPA) axis. CRH is the most proximal element of the HPA axis, and it acts as a central coordinator for neuroendocrine and behavioral responses to stress. To examine the probability of an HPA equivalent pathway in sebaceous glands, Zouboulis et al. (2002) investigated the expression of CRH, CRH-binding protein, CRHBP (OMIM Ref. No. 122559), and CRH receptors (CRHR1, 122561 and CRHR2, 602034) in sebocytes in vitro and their regulation by CRH and several other hormones. CRHR1 was the predominant type, being twice as abundant as CRHR2. CRH was biologically active on human sebocytes; it induced biphasic in-

crease in synthesis of sebaceous lipids, although it did not affect cell viability, cell proliferation, or IL1B (OMIM Ref. No. 147720)–induced IL8 (OMIM Ref. No. 146930) release. Zouboulis et al. (2002) interpreted these and other findings as indicating that CRH may be an autocrine hormone for human sebocytes that exerts homeostatic lipogenic activity, whereas testosterone and growth hormone induced CRH negative feedback. The findings implicated CRH in the clinical development of acne, seborrhea, androgenetic alopecia, skin aging, xerosis, and other skin disorders associated with alterations in lipid formation of sebaceous origin. Animal model experiments lend further support to the function of CRH. In adult male rhesus macaques, Habib et al. (2000) evaluated the effects of a lipophilic nonpeptide antagonist to CRH type 1 receptor, antalarmin, on the behavioral, neuroendocrine, and autonomic components of the stress response. After oral administration, significant antalarmin concentrations were detected in the systemic circulation and the cerebrospinal fluid. The monkeys were exposed to an intense social stressor, namely, placement of 2 unfamiliar males in adjacent cages separated only by a transparent Plexiglas screen. Antalarmin significantly inhibited a repertoire of

behaviors associated with anxiety and fear, such as body tremors, grimacing, teeth gnashing, urination, and defecation. In contrast, antalarmin increased exploratory and sexual behaviors that are normally suppressed during stress. Moreover, antalarmin significantly diminished the increases in cerebrospinal fluid CRH as well as the pituitary–adrenal, sympathetic, and adrenal medullary responses to stress. Habib et al. (2000) suggested that a CRH type 1 receptor antagonist may be of therapeutic value in human psychiatric, reproductive, and cardiovascular disorders associated with CRH system hyperactivity.

[50495] It is appreciated that the abovementioned animal model for CRH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[50496] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50497] Knapp, L. T.; Keegan, C. E.; Seasholtz, A. F.; Camper, S. A. : Corticotropin–releasing hormone (Crh) maps to mouse chromosome 3. *Mammalian Genome* 4: 615–617, 1993. ; and

[50498] Habib, K. E.; Weld, K. P.; Rice, K. C.; Pushkas, J.; Cham–

poux, M.; Listwak, S.; Webster, E. L.; Atkinson, A. J.; Schulkin, J.; Contoreggi, C.; Chrousos, G. P.; McCann, S. M.; Suomi, S. J.

[50499] Further studies establishing the function and utilities of CRH are found in John Hopkins OMIM database record ID 122560, and in cited publications numbered 196 and 2034–1983 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Development and Differentiation Enhancing Factor 1 (DDEF1, Accession XM_005169) is another VGAM1453 host target gene. DDEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDEF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDEF1 BINDING SITE, designated SEQ ID:29963, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50500] Another function of VGAM1453 is therefore inhibition of Development and Differentiation Enhancing Factor 1 (DDEF1, Accession XM_005169). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with DDEF1. Deoxyribonuclease II, Lysosomal (DNASE2, Accession NM_001375) is another VGAM1453 host target gene. DNASE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNASE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNASE2 BINDING SITE, designated SEQ ID:7048, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50501] Another function of VGAM1453 is therefore inhibition of Deoxyribonuclease II, Lysosomal (DNASE2, Accession NM_001375), a gene which has a possible role in apoptosis. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNASE2. The function of DNASE2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM885. Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 5 (SLC9A5, Accession XM_007868) is another VGAM1453

host target gene. SLC9A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC9A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A5 BINDING SITE, designated SEQ ID:30062, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50502] Another function of VGAM1453 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 5 (SLC9A5, Accession XM_007868). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A5. Von Hippel-Lindau Syndrome (VHL, Accession NM_000551) is another VGAM1453 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6159, to the nucleotide sequence of VGAM1453 RNA, herein designated

VGAM RNA, also designated SEQ ID:4164.

[50503] Another function of VGAM1453 is therefore inhibition of Von Hippel–Lindau Syndrome (VHL, Accession NM_000551), a gene which may control rna stability through the selective degradation of rna–bound proteins. Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM197. ADP–ribosylation Factor GTPase Activating Protein 1 (ARFGAP1, Accession NM_018209) is another VGAM1453 host target gene. ARFGAP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARFGAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARFGAP1 BINDING SITE, designated SEQ ID:20107, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50504] Another function of VGAM1453 is therefore inhibition of

ADP-ribosylation Factor GTPase Activating Protein 1 (ARFGAP1, Accession NM_018209). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARFGAP1. Cyclin M2 (CNNM2, Accession NM_017649) is another VGAM1453 host target gene. CNNM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM2 BINDING SITE, designated SEQ ID:19153, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50505] Another function of VGAM1453 is therefore inhibition of Cyclin M2 (CNNM2, Accession NM_017649). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM2. DKFZp547D155 (Accession XM_046977) is another VGAM1453 host target gene. DKFZp547D155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547D155, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547D155 BINDING SITE, designated SEQ ID:34868, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50506] Another function of VGAM1453 is therefore inhibition of DKFZp547D155 (Accession XM_046977). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547D155. DKFZP564B1023 (Accession NM_031306) is another VGAM1453 host target gene. DKFZP564B1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564B1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564B1023 BINDING SITE, designated SEQ ID:25341, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50507] Another function of VGAM1453 is therefore inhibition of DKFZP564B1023 (Accession NM_031306). Accordingly,

utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564B1023. FLJ12428 (Accession NM_022783) is another VGAM1453 host target gene. FLJ12428 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12428 BINDING SITE, designated SEQ ID:23066, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50508] Another function of VGAM1453 is therefore inhibition of FLJ12428 (Accession NM_022783). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12428. FLJ20694 (Accession NM_017928) is another VGAM1453 host target gene. FLJ20694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20694

BINDING SITE, designated SEQ ID:19607, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50509] Another function of VGAM1453 is therefore inhibition of FLJ20694 (Accession NM_017928). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20694. FLJ22693 (Accession NM_022750) is another VGAM1453 host target gene. FLJ22693 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22693 BINDING SITE, designated SEQ ID:22974, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50510] Another function of VGAM1453 is therefore inhibition of FLJ22693 (Accession NM_022750). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22693. KIAA0972 (Accession NM_014930) is another VGAM1453 host target gene. KIAA0972 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0972 BINDING SITE, designated SEQ ID:17226, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50511] Another function of VGAM1453 is therefore inhibition of KIAA0972 (Accession NM_014930). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0972. KIAA1056 (Accession NM_014894) is another VGAM1453 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17047, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50512] Another function of VGAM1453 is therefore inhibition of

KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. KIAA1871 (Accession XM_028409) is another VGAM1453 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30704, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50513] Another function of VGAM1453 is therefore inhibition of KIAA1871 (Accession XM_028409). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. MAN1 (Accession NM_014319) is another VGAM1453 host target gene. MAN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of MAN1 BINDING SITE, designated SEQ ID:15616, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50514] Another function of VGAM1453 is therefore inhibition of MAN1 (Accession NM_014319). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1. Mitochondrial Ribosomal Protein S18B (MRPS18B, Accession NM_014046) is another VGAM1453 host target gene. MRPS18B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS18B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS18B BINDING SITE, designated SEQ ID:15274, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50515] Another function of VGAM1453 is therefore inhibition of Mitochondrial Ribosomal Protein S18B (MRPS18B, Accession NM_014046). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with MRPS18B. ZAK (Accession NM_133646) is another VGAM1453 host target gene. ZAK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZAK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZAK BINDING SITE, designated SEQ ID:28605, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50516] Another function of VGAM1453 is therefore inhibition of ZAK (Accession NM_133646). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZAK. LOC142779 (Accession XM_084337) is another VGAM1453 host target gene. LOC142779 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC142779, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142779 BINDING SITE, designated SEQ ID:37559, to the nucleotide sequence of VGAM1453 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4164.

[50517] Another function of VGAM1453 is therefore inhibition of LOC142779 (Accession XM_084337). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142779. LOC143381 (Accession XM_084501) is another VGAM1453 host target gene. LOC143381 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143381 BINDING SITE, designated SEQ ID:37613, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50518] Another function of VGAM1453 is therefore inhibition of LOC143381 (Accession XM_084501). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143381. LOC148823 (Accession NM_145278) is another VGAM1453 host target gene. LOC148823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148823, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148823 BINDING SITE, designated SEQ ID:29793, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50519] Another function of VGAM1453 is therefore inhibition of LOC148823 (Accession NM_145278). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148823. LOC159036 (Accession XM_099018) is another VGAM1453 host target gene. LOC159036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159036 BINDING SITE, designated SEQ ID:42052, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50520] Another function of VGAM1453 is therefore inhibition of LOC159036 (Accession XM_099018). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC159036. LOC161823 (Accession XM_091156) is another VGAM1453 host target gene. LOC161823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC161823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC161823 BINDING SITE, designated SEQ ID:40033, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50521] Another function of VGAM1453 is therefore inhibition of LOC161823 (Accession XM_091156). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161823. LOC203350 (Accession XM_117536) is another VGAM1453 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43532, to

the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50522] Another function of VGAM1453 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC257464 (Accession XM_116972) is another VGAM1453 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43165, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50523] Another function of VGAM1453 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC257482 (Accession XM_168544) is another VGAM1453 host target gene. LOC257482 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257482 BINDING SITE, designated SEQ ID:45235, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50524] Another function of VGAM1453 is therefore inhibition of LOC257482 (Accession XM_168544). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257482. LOC90288 (Accession XM_030669) is another VGAM1453 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31113, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50525] Another function of VGAM1453 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities

of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. LOC92228 (Accession XM_043731) is another VGAM1453 host target gene. LOC92228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92228 BINDING SITE, designated SEQ ID:34003, to the nucleotide sequence of VGAM1453 RNA, herein designated VGAM RNA, also designated SEQ ID:4164.

[50526] Another function of VGAM1453 is therefore inhibition of LOC92228 (Accession XM_043731). Accordingly, utilities of VGAM1453 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92228. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1454 (VGAM1454) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50527] VGAM1454 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1454 was detected is described hereinabove with reference to Figs. 1–8.

[50528] VGAM1454 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50529] VGAM1454 gene encodes a VGAM1454 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1454 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1454 precursor RNA is designated SEQ ID:1440, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1440 is located at position 41662 relative to the genome of Equine Herpesvirus 2.

[50530] VGAM1454 precursor RNA folds onto itself, forming VGAM1454 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50531] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1454 folded precursor RNA into VGAM1454 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1454 RNA is designated SEQ ID:4165, and is provided hereinbelow with reference to the sequence listing part.

[50532] VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1454 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[50533] VGAM1454 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1454 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1454 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50534] The complementary binding of VGAM1454 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1454 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1454 host target RNA into VGAM1454 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50535] It is appreciated that VGAM1454 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1454 host target genes. The mRNA of each one of this plurality of VGAM1454 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1454 RNA, herein designated VGAM RNA, and which when bound by VGAM1454 RNA causes inhibition of translation of respective one or more VGAM1454 host target proteins.

[50536] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1454 gene, herein designated VGAM GENE, on one or more VGAM1454 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50537] It is yet further appreciated that a function of VGAM1454 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1454 correlate with, and may be deduced from, the identity of the host target genes which VGAM1454 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50538] Nucleotide sequences of the VGAM1454 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1454 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1454 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1454 are further
described hereinbelow with reference to Table 1.

[50539] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1454 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1454 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[50540] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1454 gene, herein designated VGAM is
inhibition of expression of VGAM1454 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1454 correlate with, and may be deduced
from, the identity of the target genes which VGAM1454
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[50541] CD244 (Accession NM_016382) is a VGAM1454 host tar-
get gene. CD244 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by CD244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD244 BINDING SITE, designated SEQ ID:18524, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50542] A function of VGAM1454 is therefore inhibition of CD244 (Accession NM_016382), a gene which can interfere with a step as proximal as phosphorylation of an activation receptor. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD244. The function of CD244 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1224. Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM_006042) is another VGAM1454 host target gene. HS3ST3A1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HS3ST3A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS3ST3A1 BINDING SITE, designated SEQ ID:12679, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50543] Another function of VGAM1454 is therefore inhibition of Heparan Sulfate (glucosamine) 3-O-sulfotransferase 3A1 (HS3ST3A1, Accession NM_006042), a gene which plays a role in the generation of heparan sulfate proteoglycan. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS3ST3A1. The function of HS3ST3A1 has been established by previous studies. Heparan sulfate biosynthetic enzymes are key components in generating a myriad of distinct heparan sulfate fine structures that carry out multiple biologic activities. The heparan sulfate D-glucosaminyl 3-O-sulfotransferases (3OSTs) place the rare 3-O-sulfate group in various sequence contexts. See 3OST2 (OMIM Ref. No. 604056). Shworak et al. (1999) isolated cDNAs encoding 3OST2, 3OST3A1, 3OST3B1 (OMIM Ref. No. 604058), and 3OST4 (OMIM Ref. No. 604059). Like 3OST2 and 3OST3B1, the predicted 406-amino acid 3OST3A1 protein is a predicted

type II integral membrane protein. Although the 3OST2 and 3OST3 enzymes have a similar regional organization, the only region of significant sequence homology occurs in the sulfotransferase domains. On the DNA level, the coding regions for the 3OST3A1 and 3OST3B1 sulfotransferase domains are nearly identical, and they share approximately 72% identity with those of 3OST2 and 3OST4. Southern blot analysis revealed that the human genome contains 2 copies of the 3OST3A and 3OST3B genes. The authors stated that they were unable to assess the functionality of the duplicate genes, which they named 3OST3A2 and 3OST3B2. Northern blot analysis revealed that the 3OST3A gene was widely expressed as multiple transcripts, with the most abundant expression in heart and placenta. In a companion paper, Liu et al. (1999) demonstrated that while the 3OST1, 3OST2, and 3OST3 isoforms each generate unique 3-O-sulfated structures, the 3OST3A and 3OST3B isoforms sulfate an identical disaccharide. Shworak et al. (1999) concluded that the 3OST multigene family encodes key enzymes that regulate the production of many distinct heparan sulfate fine structures. By inclusion within mapped clones, Shworak et al. (1999) mapped the 3OST3A1 and 3OST3B1 genes to

17p12–p11.2. Using interspecific backcross analysis, they mapped the mouse 3Ost3A and 3Ost3B genes to chromosome 11. Shworak et al. (1999) stated that the tight linkage between the 2 genes in the mouse genome suggests that they arose by a tandem duplication.

[50544] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50545] Liu, J.; Shworak, N. W.; Sinay, P.; Schwartz, J. J.; Zhang, L.; Fritze, L. M.; Rosenberg, R. D. : Expression of heparan sulfate D–glucosaminyl 3–O–sulfotransferase isoforms reveals novel substrate specificities. J. Biol. Chem. 274: 5185–5192, 1999. ; and

[50546] Shworak, N. W.; Liu, J.; Petros, L. M.; Zhang, L.; Kobayashi, M.; Copeland, N. G.; Jenkins, N. A.; Rosenberg, R. D. : Multiple isoforms of heparan sulfate D–glucosaminyl 3–O–sulfotransfera.

[50547] Further studies establishing the function and utilities of HS3ST3A1 are found in John Hopkins OMIM database record ID 604057, and in cited publications numbered 5054–5055 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Periaxin (PRX, Accession NM_020956) is another VGAM1454 host

target gene. PRX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRX BINDING SITE, designated SEQ ID:21933, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50548] Another function of VGAM1454 is therefore inhibition of Periaxin (PRX, Accession NM_020956), a gene which seems to be required for maintenance of peripheral nerve myelin sheath. may have a role in axon-glial interactions, possibly by interacting with the cytoplasmic domains of integral membrane proteins such as myelin-associated glycoprotein in the periaxonal regions of the schwann cell plasma membrane. may have a role in the early phases of myelin deposition. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRX. The function of PRX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM476.RAS, Dexamethasone-induced 1 (RASD1, Accession

NM_016084) is another VGAM1454 host target gene. RASD1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RASD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASD1 BINDING SITE, designated SEQ ID:18168, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50549] Another function of VGAM1454 is therefore inhibition of RAS, Dexamethasone-induced 1 (RASD1, Accession NM_016084), a gene which is a novel physiologic NO effector. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASD1. The function of RASD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM168. Solute Carrier Family 4, Sodium Bicarbonate Transporter-like, Member 10 (SLC4A10, Accession NM_022058) is another VGAM1454 host target gene. SLC4A10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by SLC4A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A10 BINDING SITE, designated SEQ ID:22594, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50550] Another function of VGAM1454 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Transporter-like, Member 10 (SLC4A10, Accession NM_022058). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A10. Sphingosine Kinase 2 (SPHK2, Accession NM_020126) is another VGAM1454 host target gene. SPHK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPHK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPHK2 BINDING SITE, designated SEQ ID:21312, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50551] Another function of VGAM1454 is therefore inhibition of Sphingosine Kinase 2 (SPHK2, Accession NM_020126). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPHK2. Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase) (TGM2, Accession NM_004613) is another VGAM1454 host target gene. TGM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGM2 BINDING SITE, designated SEQ ID:10952, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50552] Another function of VGAM1454 is therefore inhibition of Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase) (TGM2, Accession NM_004613), a gene which catalyzes the cross-linking of proteins and the conjugation of polyamines to proteins. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with TGM2. The function of TGM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM899. Zinc Finger Protein 278 (ZNF278, Accession NM_032052) is another VGAM1454 host target gene. ZNF278 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF278, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF278 BINDING SITE, designated SEQ ID:25783, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50553] Another function of VGAM1454 is therefore inhibition of Zinc Finger Protein 278 (ZNF278, Accession NM_032052), a gene which represses basal transcription as well as RNF4-mediated activation. Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF278. The function of ZNF278 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with

reference to VGAM414.APCL (Accession NM_005883) is another VGAM1454 host target gene. APCL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APCL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APCL BINDING SITE, designated SEQ ID:12497, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50554] Another function of VGAM1454 is therefore inhibition of APCL (Accession NM_005883). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APCL. CGRP-RCP (Accession NM_014478) is another VGAM1454 host target gene. CGRP-RCP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGRP-RCP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGRP-RCP BINDING SITE, designated SEQ ID:15822, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA,

also designated SEQ ID:4165.

[50555] Another function of VGAM1454 is therefore inhibition of CGRP-RCP (Accession NM_014478). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGRP-RCP. DKFZP564M182 (Accession XM_085525) is another VGAM1454 host target gene. DKFZP564M182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564M182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564M182 BINDING SITE, designated SEQ ID:38218, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50556] Another function of VGAM1454 is therefore inhibition of DKFZP564M182 (Accession XM_085525). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564M182. KIAA1171 (Accession XM_113868) is another VGAM1454 host target gene. KIAA1171 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by KIAA1171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1171 BINDING SITE, designated SEQ ID:42482, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50557] Another function of VGAM1454 is therefore inhibition of KIAA1171 (Accession XM_113868). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1171. Lipase, Endothelial (LIPG, Accession NM_006033) is another VGAM1454 host target gene. LIPG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIPG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPG BINDING SITE, designated SEQ ID:12654, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50558] Another function of VGAM1454 is therefore inhibition of Lipase, Endothelial (LIPG, Accession NM_006033). Accord-

ingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPG. MGC10715 (Accession NM_024325) is another VGAM1454 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23615, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50559] Another function of VGAM1454 is therefore inhibition of MGC10715 (Accession NM_024325). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. MGC4504 (Accession NM_024111) is another VGAM1454 host target gene. MGC4504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4504

BINDING SITE, designated SEQ ID:23560, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50560] Another function of VGAM1454 is therefore inhibition of MGC4504 (Accession NM_024111). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4504. LOC142955 (Accession XM_084389) is another VGAM1454 host target gene. LOC142955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC142955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142955 BINDING SITE, designated SEQ ID:37572, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50561] Another function of VGAM1454 is therefore inhibition of LOC142955 (Accession XM_084389). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142955. LOC165257 (Accession XM_092478) is another VGAM1454 host target gene. LOC165257 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165257 BINDING SITE, designated SEQ ID:40128, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50562] Another function of VGAM1454 is therefore inhibition of LOC165257 (Accession XM_092478). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165257. LOC91266 (Accession XM_037268) is another VGAM1454 host target gene. LOC91266 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91266 BINDING SITE, designated SEQ ID:32601, to the nucleotide sequence of VGAM1454 RNA, herein designated VGAM RNA, also designated SEQ ID:4165.

[50563] Another function of VGAM1454 is therefore inhibition of

LOC91266 (Accession XM_037268). Accordingly, utilities of VGAM1454 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91266. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1455 (VGAM1455) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50564] VGAM1455 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1455 was detected is described hereinabove with reference to Figs. 1-8.

[50565] VGAM1455 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50566] VGAM1455 gene encodes a VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1455 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1455 precursor RNA is designated SEQ ID:1441, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1441 is located at position 42997 relative to the genome of Equine Herpesvirus 2.

- [50567] VGAM1455 precursor RNA folds onto itself, forming VGAM1455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [50568] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1455 folded precursor RNA into VGAM1455 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide se-

quence of VGAM1455 RNA is designated SEQ ID:4166, and is provided hereinbelow with reference to the sequence listing part.

[50569] VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1455 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50570] VGAM1455 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1455 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1455 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[50571] The complementary binding of VGAM1455 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1455 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1455 host target RNA into VGAM1455 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50572] It is appreciated that VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1455 host target genes. The mRNA of each one of this plurality of VGAM1455 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1455 RNA, herein designated VGAM RNA, and which when bound by VGAM1455 RNA causes inhibition of translation of respective one or more VGAM1455 host target proteins.

[50573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1455 gene, herein designated VGAM GENE, on one or more VGAM1455 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50574] It is yet further appreciated that a function of VGAM1455

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1455 correlate with, and may be deduced from, the identity of the host target genes which VGAM1455 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50575] Nucleotide sequences of the VGAM1455 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1455 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1455 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1455 are further described hereinbelow with reference to Table 1.

[50576] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1455 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1455 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50577] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1455 gene, herein designated VGAM is inhibition of expression of VGAM1455 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1455 correlate with, and may be deduced from, the identity of the target genes which VGAM1455 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50578] Vitamin D (1,25– dihydroxyvitamin D3) Receptor (VDR, Accession NM_000376) is a VGAM1455 host target gene. VDR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VDR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDR BINDING SITE, designated SEQ ID:5946, to the nucleotide sequence of VGAM1455 RNA, herein designated VGAM RNA, also designated SEQ ID:4166.

[50579] A function of VGAM1455 is therefore inhibition of Vitamin D (1,25– dihydroxyvitamin D3) Receptor (VDR, Accession NM_000376). Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDR. FLJ20281 (Accession

XM_165663) is another VGAM1455 host target gene. FLJ20281 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20281 BINDING SITE, designated SEQ ID:43726, to the nucleotide sequence of VGAM1455 RNA, herein designated VGAM RNA, also designated SEQ ID:4166.

[50580] Another function of VGAM1455 is therefore inhibition of FLJ20281 (Accession XM_165663). Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20281. Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832) is another VGAM1455 host target gene. SLC26A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC26A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A7 BINDING SITE, designated SEQ ID:27416, to the nucleotide sequence of VGAM1455 RNA,

herein designated VGAM RNA, also designated SEQ ID:4166.

[50581] Another function of VGAM1455 is therefore inhibition of Solute Carrier Family 26, Member 7 (SLC26A7, Accession NM_052832). Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A7. LOC134266 (Accession XM_059701) is another VGAM1455 host target gene. LOC134266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC134266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134266 BINDING SITE, designated SEQ ID:37067, to the nucleotide sequence of VGAM1455 RNA, herein designated VGAM RNA, also designated SEQ ID:4166.

[50582] Another function of VGAM1455 is therefore inhibition of LOC134266 (Accession XM_059701). Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134266. LOC144438 (Accession XM_084860) is another VGAM1455 host target gene. LOC144438 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144438 BINDING SITE, designated SEQ ID:37736, to the nucleotide sequence of VGAM1455 RNA, herein designated VGAM RNA, also designated SEQ ID:4166.

[50583] Another function of VGAM1455 is therefore inhibition of LOC144438 (Accession XM_084860). Accordingly, utilities of VGAM1455 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144438. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1456 (VGAM1456) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50584] VGAM1456 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1456 was detected is described hereinabove with reference to Figs. 1-8.

[50585] VGAM1456 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50586] VGAM1456 gene encodes a VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1456 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1456 precursor RNA is designated SEQ ID:1442, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1442 is located at position 39288 relative to the genome of Equine Herpesvirus 2.

[50587] VGAM1456 precursor RNA folds onto itself, forming VGAM1456 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[50588] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1456 folded precursor RNA into VGAM1456 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1456 RNA is designated SEQ ID:4167, and is provided hereinbelow with reference to the sequence listing part.

[50589] VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1456 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50590] VGAM1456 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1456 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1456 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1456 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[50591] The complementary binding of VGAM1456 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1456 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1456 host target RNA into VGAM1456 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50592] It is appreciated that VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1456 host target genes. The mRNA of each one of this plurality of VGAM1456 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1456 RNA, herein designated VGAM RNA, and which when bound by VGAM1456 RNA causes inhibition of translation of respective one or more VGAM1456 host target proteins.

[50593] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1456 gene, herein designated VGAM GENE, on one or more VGAM1456 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50594] It is yet further appreciated that a function of VGAM1456 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1456 correlate with, and may be deduced from, the identity of the host target genes which VGAM1456 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50595] Nucleotide sequences of the VGAM1456 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1456 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1456 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1456 are further described hereinbelow with reference to Table 1.

[50596] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1456 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1456 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50597] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1456 gene, herein designated VGAM is inhibition of expression of VGAM1456 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1456 correlate with, and may be deduced from, the identity of the target genes which VGAM1456 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50598] Fatty-acid-Coenzyme A Ligase, Long-chain 2 (FACL2, Accession NM_021122) is a VGAM1456 host target gene. FACL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FACL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of FACL2 BINDING SITE, designated SEQ ID:22096, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50599] A function of VGAM1456 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 2 (FACL2, Accession NM_021122), a gene which activates long-chain fatty acids for both synthesis of cellular lipids. Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL2. The function of FACL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is another VGAM1456 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ

ID:28936, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50600] Another function of VGAM1456 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. ARL8 (Accession XM_167671) is another VGAM1456 host target gene. ARL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARL8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARL8 BINDING SITE, designated SEQ ID:44760, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50601] Another function of VGAM1456 is therefore inhibition of ARL8 (Accession XM_167671). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARL8. DKFZp547H025 (Accession NM_020161) is another

VGAM1456 host target gene. DKFZp547H025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547H025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547H025 BINDING SITE, designated SEQ ID:21370, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50602] Another function of VGAM1456 is therefore inhibition of DKFZp547H025 (Accession NM_020161). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547H025. DKFZP761F241 (Accession NM_031455) is another VGAM1456 host target gene. DKFZP761F241 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761F241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761F241 BINDING SITE, designated SEQ ID:25476, to the nucleotide sequence of

VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50603] Another function of VGAM1456 is therefore inhibition of DKFZP761F241 (Accession NM_031455). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761F241. FLJ13881 (Accession NM_024729) is another VGAM1456 host target gene. FLJ13881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13881 BINDING SITE, designated SEQ ID:24068, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50604] Another function of VGAM1456 is therefore inhibition of FLJ13881 (Accession NM_024729). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13881. FLJ22644 (Accession NM_025098) is another VGAM1456 host target gene. FLJ22644 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ22644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22644 BINDING SITE, designated SEQ ID:24740, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50605] Another function of VGAM1456 is therefore inhibition of FLJ22644 (Accession NM_025098). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22644. KIAA0258 (Accession NM_014785) is another VGAM1456 host target gene. KIAA0258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0258 BINDING SITE, designated SEQ ID:16644, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50606] Another function of VGAM1456 is therefore inhibition of KIAA0258 (Accession NM_014785). Accordingly, utilities

of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0258. KIAA0296 (Accession NM_014699) is another VGAM1456 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16217, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50607] Another function of VGAM1456 is therefore inhibition of KIAA0296 (Accession NM_014699). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. KIAA1100 (Accession NM_014901) is another VGAM1456 host target gene. KIAA1100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1100 BINDING SITE, designated SEQ ID:17083, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50608] Another function of VGAM1456 is therefore inhibition of KIAA1100 (Accession NM_014901). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1100. Solute Carrier Family 25 (mitochondrial oxodicarboxylate carrier), Member 21 (SLC25A21, Accession NM_030631) is another VGAM1456 host target gene. SLC25A21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC25A21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC25A21 BINDING SITE, designated SEQ ID:24966, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50609] Another function of VGAM1456 is therefore inhibition of Solute Carrier Family 25 (mitochondrial oxodicarboxylate carrier), Member 21 (SLC25A21, Accession NM_030631). Accordingly, utilities of VGAM1456 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with SLC25A21. LOC149372 (Accession XM_086509) is another VGAM1456 host target gene.

LOC149372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38729, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50610] Another function of VGAM1456 is therefore inhibition of LOC149372 (Accession XM_086509). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC154860 (Accession XM_098623) is another VGAM1456 host target gene. LOC154860 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC154860 BINDING SITE, designated SEQ ID:41735, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50611] Another function of VGAM1456 is therefore inhibition of LOC154860 (Accession XM_098623). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154860. LOC197358 (Accession XM_113872) is another VGAM1456 host target gene. LOC197358 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197358 BINDING SITE, designated SEQ ID:42505, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50612] Another function of VGAM1456 is therefore inhibition of LOC197358 (Accession XM_113872). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197358. LOC257177 (Accession XM_170909) is another VGAM1456 host target gene. LOC257177 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257177 BINDING SITE, designated SEQ ID:45675, to the nucleotide sequence of VGAM1456 RNA, herein designated VGAM RNA, also designated SEQ ID:4167.

[50613] Another function of VGAM1456 is therefore inhibition of LOC257177 (Accession XM_170909). Accordingly, utilities of VGAM1456 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257177. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1457 (VGAM1457) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50614] VGAM1457 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1457 was detected is described hereinabove with reference to Figs. 1-8.

[50615] VGAM1457 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50616] VGAM1457 gene encodes a VGAM1457 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1457 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1457 precursor RNA is designated SEQ ID:1443, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1443 is located at position 43126 relative to the genome of Equine Herpesvirus 2.

[50617] VGAM1457 precursor RNA folds onto itself, forming VGAM1457 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[50618] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1457 folded precursor RNA into VGAM1457 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1457 RNA is designated SEQ ID:4168, and is provided hereinbelow with reference to the sequence listing part.

[50619] VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1457 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50620] VGAM1457 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1457 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1457 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1457 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50621] The complementary binding of VGAM1457 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1457 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1457 host target RNA into VGAM1457 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50622] It is appreciated that VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1457 host target genes. The mRNA of each one of this plurality of VGAM1457 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1457 RNA, herein designated VGAM RNA, and which when bound by VGAM1457 RNA causes inhibition of translation of respective one or more VGAM1457 host target proteins.

[50623] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1457 gene, herein designated VGAM GENE, on one or more VGAM1457 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50624] It is yet further appreciated that a function of VGAM1457 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1457 correlate with, and may be deduced from, the identity of the host target genes which VGAM1457 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50625] Nucleotide sequences of the VGAM1457 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1457 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1457 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1457 are further described hereinbelow with reference to Table 1.

[50626] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1457 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1457 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50627] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1457 gene, herein designated VGAM is inhibition of expression of VGAM1457 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1457 correlate with, and may be deduced from, the identity of the target genes which VGAM1457 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50628] Zinc Finger Protein 146 (ZNF146, Accession NM_007145) is a VGAM1457 host target gene. ZNF146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ZNF146 BINDING SITE, designated SEQ ID:13993, to the nucleotide sequence of VGAM1457 RNA, herein designated VGAM RNA, also designated SEQ ID:4168.

[50629] A function of VGAM1457 is therefore inhibition of Zinc Finger Protein 146 (ZNF146, Accession NM_007145), a gene which binds zinc ions, DNA, and heparin. Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF146. The function of ZNF146 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM192.KIAA0063 (Accession NM_014876) is another VGAM1457 host target gene. KIAA0063 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0063 BINDING SITE, designated SEQ ID:17015, to the nucleotide sequence of VGAM1457 RNA, herein designated VGAM RNA, also designated SEQ ID:4168.

[50630] Another function of VGAM1457 is therefore inhibition of KIAA0063 (Accession NM_014876). Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0063. KIAA0676 (Accession NM_015043) is another VGAM1457 host target gene. KIAA0676 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0676 BINDING SITE, designated SEQ ID:17391, to the nucleotide sequence of VGAM1457 RNA, herein designated VGAM RNA, also designated SEQ ID:4168.

[50631] Another function of VGAM1457 is therefore inhibition of KIAA0676 (Accession NM_015043). Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0676. Neurexophilin 3 (NXPH3, Accession XM_037847) is another VGAM1457 host target gene. NXPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXPH3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXPH3 BINDING SITE, designated SEQ ID:32711, to the nucleotide sequence of VGAM1457 RNA, herein designated VGAM RNA, also designated SEQ ID:4168.

[50632] Another function of VGAM1457 is therefore inhibition of Neurexophilin 3 (NXPH3, Accession XM_037847). Accordingly, utilities of VGAM1457 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXPH3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1458 (VGAM1458) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50633] VGAM1458 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1458 was detected is described hereinabove with reference to Figs. 1–8.

[50634] VGAM1458 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2.

VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50635] VGAM1458 gene encodes a VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1458 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1458 precursor RNA is designated SEQ ID:1444, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1444 is located at position 39736 relative to the genome of Equine Herpesvirus 2.

[50636] VGAM1458 precursor RNA folds onto itself, forming VGAM1458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50637] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM1458 folded precursor RNA into VGAM1458 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1458 RNA is designated SEQ ID:4169, and is provided hereinbelow with reference to the sequence listing part.

[50638] VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1458 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50639] VGAM1458 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM1458 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1458 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50640] The complementary binding of VGAM1458 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1458 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1458 host target RNA into VGAM1458 host target protein,

herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50641] It is appreciated that VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1458 host target genes. The mRNA of each one of this plurality of VGAM1458 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1458 RNA, herein designated VGAM RNA, and which when bound by VGAM1458 RNA causes inhibition of translation of respective one or more VGAM1458 host target proteins.

[50642] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1458 gene, herein designated VGAM GENE, on one or more VGAM1458 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50643] It is yet further appreciated that a function of VGAM1458 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1458 correlate with, and may be deduced from, the identity of the host target genes which VGAM1458 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50644] Nucleotide sequences of the VGAM1458 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1458 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1458 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1458 are further described hereinbelow with reference to Table 1.

[50645] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1458 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1458 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50646] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1458 gene, herein designated VGAM is inhibition of expression of VGAM1458 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1458 correlate with, and may be deduced from, the identity of the target genes which VGAM1458 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50647] Calcitonin Receptor-like (CALCRL, Accession NM_005795) is a VGAM1458 host target gene. CALCRL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALCRL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALCRL BINDING SITE, designated SEQ ID:12375, to the nucleotide

sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50648] A function of VGAM1458 is therefore inhibition of Calcitonin Receptor-like (CALCRL, Accession NM_005795), a gene which is a receptor for calcitonin gene-related peptide type 1. Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALCRL. The function of CALCRL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM995. Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM_052988) is another VGAM1458 host target gene. CDK10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK10 BINDING SITE, designated SEQ ID:27553, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50649] Another function of VGAM1458 is therefore inhibition of

Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM_052988), a gene which plays a pivotal role in the regulation of the eukaryotic cell cycle. Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK10. The function of CDK10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193.A Disintegrin and Metalloproteinase Domain 9 (meltrin gamma) (ADAM9, Accession NM_003816) is another VGAM1458 host target gene. ADAM9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM9 BINDING SITE, designated SEQ ID:9905, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50650] Another function of VGAM1458 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 9 (meltrin gamma) (ADAM9, Accession NM_003816). Accordingly,

utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM9. KIAA1164 (Accession XM_045358) is another VGAM1458 host target gene. KIAA1164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1164 BINDING SITE, designated SEQ ID:34439, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50651] Another function of VGAM1458 is therefore inhibition of KIAA1164 (Accession XM_045358). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1164. KIAA1211 (Accession XM_044178) is another VGAM1458 host target gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1211 BINDING SITE, designated SEQ ID:34158, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50652] Another function of VGAM1458 is therefore inhibition of KIAA1211 (Accession XM_044178). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. KIAA1458 (Accession XM_044434) is another VGAM1458 host target gene. KIAA1458 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1458, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1458 BINDING SITE, designated SEQ ID:34202, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50653] Another function of VGAM1458 is therefore inhibition of KIAA1458 (Accession XM_044434). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1458. MGC5566 (Accession NM_024049) is another VGAM1458 host target gene. MGC5566 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5566 BINDING SITE, designated SEQ ID:23485, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50654] Another function of VGAM1458 is therefore inhibition of MGC5566 (Accession NM_024049). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5566. PANK (Accession NM_138316) is another VGAM1458 host target gene. PANK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PANK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PANK BINDING SITE, designated SEQ ID:28714, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50655] Another function of VGAM1458 is therefore inhibition of

PANK (Accession NM_138316). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PANK. LOC146667 (Accession XM_097044) is another VGAM1458 host target gene. LOC146667 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146667 BINDING SITE, designated SEQ ID:40710, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50656] Another function of VGAM1458 is therefore inhibition of LOC146667 (Accession XM_097044). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146667. LOC147184 (Accession NM_145274) is another VGAM1458 host target gene. LOC147184 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC147184 BINDING SITE, designated SEQ ID:29786, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50657] Another function of VGAM1458 is therefore inhibition of LOC147184 (Accession NM_145274). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147184. LOC149448 (Accession XM_097642) is another VGAM1458 host target gene. LOC149448 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149448 BINDING SITE, designated SEQ ID:40989, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50658] Another function of VGAM1458 is therefore inhibition of LOC149448 (Accession XM_097642). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149448. LOC200531 (Accession XM_114244) is an-

other VGAM1458 host target gene. LOC200531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200531 BINDING SITE, designated SEQ ID:42817, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50659] Another function of VGAM1458 is therefore inhibition of LOC200531 (Accession XM_114244). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200531. LOC257443 (Accession XM_171072) is another VGAM1458 host target gene. LOC257443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257443 BINDING SITE, designated SEQ ID:45871, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50660] Another function of VGAM1458 is therefore inhibition of LOC257443 (Accession XM_171072). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257443. LOC51301 (Accession NM_016591) is another VGAM1458 host target gene. LOC51301 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC51301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51301 BINDING SITE, designated SEQ ID:18669, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50661] Another function of VGAM1458 is therefore inhibition of LOC51301 (Accession NM_016591). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51301. LOC90110 (Accession XM_029046) is another VGAM1458 host target gene. LOC90110 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90110, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90110 BINDING SITE, designated SEQ ID:30840, to the nucleotide sequence of VGAM1458 RNA, herein designated VGAM RNA, also designated SEQ ID:4169.

[50662] Another function of VGAM1458 is therefore inhibition of LOC90110 (Accession XM_029046). Accordingly, utilities of VGAM1458 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90110. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1459 (VGAM1459) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50663] VGAM1459 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1459 was detected is described hereinabove with reference to Figs. 1-8.

[50664] VGAM1459 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1459 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[50665] VGAM1459 gene encodes a VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1459 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1459 precursor RNA is designated SEQ ID:1445, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1445 is located at position 39156 relative to the genome of Equine Herpesvirus 2.

[50666] VGAM1459 precursor RNA folds onto itself, forming VGAM1459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50667] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1459 folded precursor RNA into VGAM1459

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1459 RNA is designated SEQ ID:4170, and is provided hereinbelow with reference to the sequence listing part.

[50668] VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1459 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50669] VGAM1459 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1459 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1459 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50670] The complementary binding of VGAM1459 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1459 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1459 host target RNA into VGAM1459 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[50671] It is appreciated that VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1459 host target genes. The mRNA of each one of this plurality of VGAM1459 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1459 RNA, herein designated VGAM RNA, and which when bound by VGAM1459 RNA causes inhibition of translation of respective one or more VGAM1459 host target proteins.

[50672] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1459 gene, herein designated VGAM GENE, on one or more VGAM1459 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50673] It is yet further appreciated that a function of VGAM1459 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1459 correlate with, and may be deduced from, the identity of the host target genes which VGAM1459 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50674] Nucleotide sequences of the VGAM1459 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1459 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1459 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1459 are further described hereinbelow with reference to Table 1.

[50675] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1459 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1459 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50676] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1459 gene, herein designated VGAM is inhibition of expression of VGAM1459 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1459 correlate with, and may be deduced from, the identity of the target genes which VGAM1459 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50677] Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM_000499) is a VGAM1459 host target gene. CYP1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A1 BINDING SITE, designated SEQ ID:6111, to the nucleotide

sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50678] A function of VGAM1459 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM_000499), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A1. The function of CYP1A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM335. Ladinin 1 (LAD1, Accession NM_005558) is another VGAM1459 host target gene. LAD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAD1 BINDING SITE, designated SEQ ID:12084, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50679] Another function of VGAM1459 is therefore inhibition of

Ladinin 1 (LAD1, Accession NM_005558). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAD1. Lipase, Hormone-sensitive (LIPE, Accession NM_005357) is another VGAM1459 host target gene. LIPE BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LIPE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPE BINDING SITE, designated SEQ ID:11825, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50680] Another function of VGAM1459 is therefore inhibition of Lipase, Hormone-sensitive (LIPE, Accession NM_005357), a gene which primarily hydrolyzes stored triglycerides to free fatty acids. Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPE. The function of LIPE has been established by previous studies. Free fatty acids (FFA) derived from adipose tissue triglycerides are the most important fuel in mammals and provide more than half the caloric needs during fasting. Hormone-sensi-

tive lipase (HSL) has a vital role in the mobilization of FFA from adipose tissue by controlling the rate of lipolysis of the stored triglycerides. HSL regulates energy homeostasis by catalyzing the rate-limiting step in adipose tissue lipolysis. Like glycogen phosphorylase (OMIM Ref. No. 232700), the corresponding enzyme in carbohydrate metabolism, HSL is under acute neuronal and hormonal control. In both cases activation by catecholamines occurs through the cyclic AMP-mediated phosphorylation of a single serine residue. The dephosphorylation of HSL by insulin is responsible for the antilipolytic effect of this hormone, one of its most important actions. Holm et al. (1988) cloned the gene for hormone-sensitive lipase from the rat adipocyte and found that the 757-amino acid sequence predicted by the cDNA shows no homology with any other known lipase or protein. The activity-controlling phosphorylation site was localized to serine-563 in a markedly hydrophilic domain, and a lipid-binding consensus site was tentatively identified. They used the rat clone to map the human HSL gene to 19cen-q13.3 by Southern analysis of DNA from human-rodent somatic cell hybrids. By hybridization studies using a panel of somatic cell hybrids with subchromosomal segments of 19q, Schonk et

al. (1990) localized the HSL gene, symbolized LIPE, to 19q13.1. By fluorescence in situ hybridization, Levitt et al. (1995) mapped the LIPE gene to 19q13.1–q13.2 Li et al. (1994) found that the gene encoding mouse Hsl spans approximately 10.4 kb and comprises 9 exons interrupted by 8 introns. The deduced amino acid sequence predicted a protein that shows 94% identity with the previously determined rat sequence and 85% identity with the human sequence. Despite the high degree of similarity, the 3 species diverge significantly for a stretch of 16 amino acid residues upstream of the phosphorylation site. Wang et al. (1994) demonstrated that the homologous gene is on proximal chromosome 7 in the mouse. The mouse locus, symbolized Lipe, was found to be distinct from the Tub and Ad loci, which are associated with obesity in the mouse

[50681] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50682] Schonk, D.; van Dijk, P.; Riegmann, P.; Trapman, J.; Holm, C.; Willcocks, T. C.; Sillekens, P.; van Venrooij, W.; Wimmer, E.; Geurts van Kessel, A.; Ropers, H.–H.; Wieringa, B. : Assignment of seven genes to distinct intervals on the

midportion of human chromosome 19q surrounding the myotonic dystrophy gene region. Cytogenet. Cell Genet. 54: 15–19, 1990. ; and

[50683] Levitt, R. C.; Liu, Z.; Nouri, N.; Meyers, D. A.; Brandriff, B.; Mohrenweiser, H. M. : Mapping of the gene for hormone sensitive lipase (LIPE) to chromosome 19q13.1–q13.2. Cytogenet. Cell G.

[50684] Further studies establishing the function and utilities of LIPE are found in John Hopkins OMIM database record ID 151750, and in cited publications numbered and 3788–3793 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Supervillin (SVIL, Accession NM_003174) is another VGAM1459 host target gene. SVIL BINDING SITE1 and SVIL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SVIL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SVIL BINDING SITE1 and SVIL BINDING SITE2, designated SEQ ID:9149 and SEQ ID:22346 respectively, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50685] Another function of VGAM1459 is therefore inhibition of Supervillin (SVIL, Accession NM_003174), a gene which binds actin, links filamentous actin with the plasma membrane; and contains putative nuclear localization signals. Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SVIL. The function of SVIL has been established by previous studies. Pope et al. (1998) used PCR with primers based on bovine sequence to clone human supervillin. The human gene encodes a 1,788-amino acid polypeptide that contains 3 predicted nuclear localization signals, several consensus phosphorylation sites, 1 ATP/GTP-binding motif, 1 potential RNP-binding site, and 3 potential actin-binding sites. The region containing the actin-binding sites is similar to the 'headpiece' of villin (OMIM Ref. No. 193040). Dot blots showed that many tissues express supervillin, with the highest expression in muscle tissues. Northern blot analysis revealed a 7.5-kb mRNA that is abundant in some human cancer cell lines. Southern blot analysis revealed that supervillin is a single-copy gene. Activation of androgen receptor (AR; 313700) via androgen in muscle cells is closely linked to their growth and differentiation. Ting et al. (2002) cloned and

characterized supervillin as an AR coregulator from a skeletal muscle cDNA library. They identified a domain within supervillin (amino acids 594 to 1,268) that could interact with the AR N terminus and DNA-binding domain–ligand-binding domain in a ligand-enhanced manner. Subcellular colocalization studies with fluorescence staining indicated that supervillin colocalized with AR in the presence of 5- α -dihydrotestosterone in COS-1 cells. Furthermore, supervillin could enhance expression of the endogenous AR target gene p27(KIP1) (OMIM Ref. No. 600778) in prostate cells. Thus, supervillin is an AR coregulator that can enhance AR transactivation in muscle and other cells.

[50686] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50687] Pope, R. K.; Pestonjamas, K. N.; Smith, K. P.; Wulfkühle, J. D.; Strassel, C. P.; Lawrence, J. B.; Luna, E. J. : Cloning, characterization, and chromosomal localization of human supervillin (SVIL). *Genomics* 52: 342–351, 1998. ; and

[50688] Ting, H.-J.; Yeh, S.; Nishimura, K.; Chang, C. : Supervillin associates with androgen receptor and modulates its transcriptional activity. *Proc. Nat. Acad. Sci.* 99: 661–666,

2002.

[50689] Further studies establishing the function and utilities of SVIL are found in John Hopkins OMIM database record ID 604126, and in cited publications numbered 7410–7411 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nudix (nucleoside diphosphate linked moiety X)–type Motif 11 (NUDT11, Accession XM_010230) is another VGAM1459 host target gene. NUDT11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT11 BINDING SITE, designated SEQ ID:30136, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50690] Another function of VGAM1459 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)–type Motif 11 (NUDT11, Accession XM_010230). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUDT11. Pleiomorphic Adenoma Gene–like 2

(PLAGL2, Accession XM_047007) is another VGAM1459 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34873, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50691] Another function of VGAM1459 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. PRO2958 (Accession NM_018546) is another VGAM1459 host target gene. PRO2958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2958 BINDING SITE, designated SEQ ID:20625, to the nucleotide sequence of VGAM1459

RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50692] Another function of VGAM1459 is therefore inhibition of PRO2958 (Accession NM_018546). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2958. LOC154790 (Accession XM_088044) is another VGAM1459 host target gene. LOC154790 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC154790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154790 BINDING SITE, designated SEQ ID:39489, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50693] Another function of VGAM1459 is therefore inhibition of LOC154790 (Accession XM_088044). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154790. LOC203197 (Accession XM_114645) is another VGAM1459 host target gene. LOC203197 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC203197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203197 BINDING SITE, designated SEQ ID:43008, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50694] Another function of VGAM1459 is therefore inhibition of LOC203197 (Accession XM_114645). Accordingly, utilities of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203197. LOC254249 (Accession XM_170931) is another VGAM1459 host target gene. LOC254249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254249 BINDING SITE, designated SEQ ID:45711, to the nucleotide sequence of VGAM1459 RNA, herein designated VGAM RNA, also designated SEQ ID:4170.

[50695] Another function of VGAM1459 is therefore inhibition of LOC254249 (Accession XM_170931). Accordingly, utilities

of VGAM1459 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1460 (VGAM1460) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50696] VGAM1460 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1460 was detected is described hereinabove with reference to Figs. 1-8.

[50697] VGAM1460 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50698] VGAM1460 gene encodes a VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1460 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1460 precursor RNA is designated SEQ ID:1446, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1446 is located at position 39460 relative to the genome of Equine Herpesvirus 2.

[50699] VGAM1460 precursor RNA folds onto itself, forming VGAM1460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50700] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1460 folded precursor RNA into VGAM1460 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1460 RNA is designated SEQ ID:4171, and

is provided hereinbelow with reference to the sequence listing part.

[50701] VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1460 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50702] VGAM1460 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1460 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1460 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50703] The complementary binding of VGAM1460 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1460 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1460 host target RNA into VGAM1460 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50704] It is appreciated that VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1460 host target genes. The mRNA of each one of this plurality of VGAM1460 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM1460 RNA, herein designated VGAM RNA, and which when bound by VGAM1460 RNA causes inhibition of translation of respective one or more VGAM1460 host target proteins.

[50705] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1460 gene, herein designated VGAM GENE, on one or more VGAM1460 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50706] It is yet further appreciated that a function of VGAM1460 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1460 correlate with, and may be deduced from, the identity of the host target genes which VGAM1460 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50707] Nucleotide sequences of the VGAM1460 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1460 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1460 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1460 are further described hereinbelow with reference to Table 1.

[50708] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1460 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1460 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50709] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1460 gene, herein designated VGAM is inhibition of expression of VGAM1460 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1460 correlate with, and may be deduced from, the identity of the target genes which VGAM1460 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50710] KIAA0237 (Accession NM_014747) is a VGAM1460 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16441, to the nucleotide sequence of VGAM1460 RNA, herein designated VGAM RNA, also designated SEQ ID:4171.

[50711] A function of VGAM1460 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0453 (Accession XM_044546) is another VGAM1460 host target gene. KIAA0453 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0453 BINDING SITE, designated SEQ ID:34229, to the nucleotide sequence of VGAM1460 RNA, herein designated VGAM RNA, also designated SEQ ID:4171.

[50712] Another function of VGAM1460 is therefore inhibition of KIAA0453 (Accession XM_044546). Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0453. MGC10812 (Accession NM_031425) is another VGAM1460 host target gene. MGC10812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10812 BINDING SITE, designated SEQ ID:25411, to the nucleotide sequence of VGAM1460 RNA, herein designated VGAM RNA, also designated SEQ ID:4171.

[50713] Another function of VGAM1460 is therefore inhibition of

MGC10812 (Accession NM_031425). Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10812. LOC219397 (Accession XM_167889) is another VGAM1460 host target gene. LOC219397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219397 BINDING SITE, designated SEQ ID:44899, to the nucleotide sequence of VGAM1460 RNA, herein designated VGAM RNA, also designated SEQ ID:4171.

[50714] Another function of VGAM1460 is therefore inhibition of LOC219397 (Accession XM_167889). Accordingly, utilities of VGAM1460 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219397. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1461 (VGAM1461) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[50715] VGAM1461 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1461 was detected is described hereinabove with reference to Figs. 1–8.

[50716] VGAM1461 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50717] VGAM1461 gene encodes a VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1461 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1461 precursor RNA is designated SEQ ID:1447, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1447 is located at position 44627 relative to the genome of Equine Herpesvirus 2.

[50718] VGAM1461 precursor RNA folds onto itself, forming VGAM1461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50719] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1461 folded precursor RNA into VGAM1461 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1461 RNA is designated SEQ ID:4172, and is provided hereinbelow with reference to the sequence listing part.

[50720] VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1461 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50721] VGAM1461 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1461 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1461 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[50722] The complementary binding of VGAM1461 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1461 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1461 host target RNA into VGAM1461 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50723] It is appreciated that VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1461 host target genes. The mRNA of each one of this plurality of VGAM1461 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1461 RNA, herein designated VGAM RNA, and which when bound by VGAM1461 RNA causes inhibition of translation of respective one or more VGAM1461 host target proteins.

[50724] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1461 gene, herein designated VGAM GENE, on one

or more VGAM1461 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50725] It is yet further appreciated that a function of VGAM1461 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1461 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1461 correlate with, and may be deduced from, the identity of the host target genes which VGAM1461 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50726] Nucleotide sequences of the VGAM1461 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1461 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1461 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1461 are further described hereinbelow with reference to Table 1.

[50727] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1461 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1461 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50728] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1461 gene, herein designated VGAM is inhibition of expression of VGAM1461 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1461 correlate with, and may be deduced from, the identity of the target genes which VGAM1461 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50729] Membrane-spanning 4-domains, Subfamily A, Member 3

(hematopoietic cell-specific) (MS4A3, Accession NM_006138) is a VGAM1461 host target gene. MS4A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MS4A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MS4A3 BINDING SITE, designated SEQ ID:12777, to the nucleotide sequence of VGAM1461 RNA, herein designated VGAM RNA, also designated SEQ ID:4172.

[50730] A function of VGAM1461 is therefore inhibition of Membrane-spanning 4-domains, Subfamily A, Member 3 (hematopoietic cell-specific) (MS4A3, Accession NM_006138). Accordingly, utilities of VGAM1461 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MS4A3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1462 (VGAM1462) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50731] VGAM1462 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1462 was detected is described hereinabove with reference to Figs. 1–8.

[50732] VGAM1462 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50733] VGAM1462 gene encodes a VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1462 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1462 precursor RNA is designated SEQ ID:1448, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1448 is located at position 40327 relative to the genome of Equine Herpesvirus 2.

[50734] VGAM1462 precursor RNA folds onto itself, forming VGAM1462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50735] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1462 folded precursor RNA into VGAM1462 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1462 RNA is designated SEQ ID:4173, and is provided hereinbelow with reference to the sequence listing part.

[50736] VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1462 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50737] VGAM1462 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1462 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1462 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50738] The complementary binding of VGAM1462 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1462 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1462 host target RNA into VGAM1462 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50739] It is appreciated that VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1462 host target genes. The mRNA of each one of this plurality of VGAM1462 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1462 RNA, herein designated VGAM RNA, and which when bound by VGAM1462 RNA causes inhibition of translation of respective one or more VGAM1462 host target proteins.

[50740] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1462 gene, herein designated VGAM GENE, on one or more VGAM1462 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50741] It is yet further appreciated that a function of VGAM1462 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1462 correlate with, and may be deduced from, the identity of the host target genes which VGAM1462 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50742] Nucleotide sequences of the VGAM1462 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1462 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1462 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1462 are further described hereinbelow with reference to Table 1.

[50743] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1462 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1462 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50744] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1462 gene, herein designated VGAM is inhibition of expression of VGAM1462 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1462 correlate with, and may be deduced from, the identity of the target genes which VGAM1462 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50745] Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila) (PDE4D, Accession XM_056815) is a VGAM1462 host target gene. PDE4D

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36437, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50746] A function of VGAM1462 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558) is another VGAM1462 host target gene. PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3 are HOST TARGET binding

sites found in untranslated regions of mRNA encoded by PPP1R8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3, designated SEQ ID:28855, SEQ ID:8569 and SEQ ID:15339 respectively, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50747] Another function of VGAM1462 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM101.KIAA0603 (Accession NM_014832) is another VGAM1462 host target gene. KIAA0603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0603, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0603 BINDING SITE, designated SEQ ID:16828, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50748] Another function of VGAM1462 is therefore inhibition of KIAA0603 (Accession NM_014832). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0603. MEGF10 (Accession NM_032446) is another VGAM1462 host target gene. MEGF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEGF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF10 BINDING SITE, designated SEQ ID:26208, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50749] Another function of VGAM1462 is therefore inhibition of MEGF10 (Accession NM_032446). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MEGF10. MGC13008 (Accession NM_032686) is another VGAM1462 host target gene. MGC13008 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC13008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13008 BINDING SITE, designated SEQ ID:26406, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50750] Another function of VGAM1462 is therefore inhibition of MGC13008 (Accession NM_032686). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13008. MGC14156 (Accession NM_032906) is another VGAM1462 host target gene. MGC14156 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC14156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14156 BINDING SITE, designated SEQ ID:26727, to

the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50751] Another function of VGAM1462 is therefore inhibition of MGC14156 (Accession NM_032906). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14156. Protocadherin 10 (PCDH10, Accession NM_032961) is another VGAM1462 host target gene. PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2, designated SEQ ID:26768 and SEQ ID:21883 respectively, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50752] Another function of VGAM1462 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM_032961). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. LOC142893 (Accession

XM_096354) is another VGAM1462 host target gene.

LOC142893 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC142893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142893 BINDING SITE, designated SEQ ID:40321, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50753] Another function of VGAM1462 is therefore inhibition of LOC142893 (Accession XM_096354). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142893. LOC148545 (Accession XM_086226) is another VGAM1462 host target gene. LOC148545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148545 BINDING SITE, designated SEQ ID:38554, to the nucleotide sequence of VGAM1462 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4173.

[50754] Another function of VGAM1462 is therefore inhibition of LOC148545 (Accession XM_086226). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148545. LOC150170 (Accession XM_086799) is another VGAM1462 host target gene. LOC150170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150170 BINDING SITE, designated SEQ ID:38862, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50755] Another function of VGAM1462 is therefore inhibition of LOC150170 (Accession XM_086799). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150170. LOC150175 (Accession XM_086806) is another VGAM1462 host target gene. LOC150175 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150175, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150175 BINDING SITE, designated SEQ ID:38884, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50756] Another function of VGAM1462 is therefore inhibition of LOC150175 (Accession XM_086806). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150175. LOC150215 (Accession XM_086813) is another VGAM1462 host target gene. LOC150215 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150215 BINDING SITE, designated SEQ ID:38888, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50757] Another function of VGAM1462 is therefore inhibition of LOC150215 (Accession XM_086813). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC150215. LOC150218 (Accession XM_086850) is another VGAM1462 host target gene. LOC150218 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150218 BINDING SITE, designated SEQ ID:38915, to the nucleotide sequence of VGAM1462 RNA, herein designated VGAM RNA, also designated SEQ ID:4173.

[50758] Another function of VGAM1462 is therefore inhibition of LOC150218 (Accession XM_086850). Accordingly, utilities of VGAM1462 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150218. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1463 (VGAM1463) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50759] VGAM1463 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1463 was detected is described hereinabove with reference to Figs. 1–8.

[50760] VGAM1463 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50761] VGAM1463 gene encodes a VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1463 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1463 precursor RNA is designated SEQ ID:1449, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1449 is located at position 38131 relative to the genome of Equine Herpesvirus 2.

[50762] VGAM1463 precursor RNA folds onto itself, forming VGAM1463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50763] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1463 folded precursor RNA into VGAM1463 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1463 RNA is designated SEQ ID:4174, and is provided hereinbelow with reference to the sequence listing part.

[50764] VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1463 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50765] VGAM1463 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1463 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1463 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50766] The complementary binding of VGAM1463 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1463 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1463 host target RNA into VGAM1463 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50767] It is appreciated that VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1463 host target genes. The mRNA of each one of this plurality of VGAM1463 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1463 RNA, herein designated VGAM RNA, and which when bound by VGAM1463 RNA causes inhibition of translation of respective one or more VGAM1463 host target proteins.

[50768] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1463 gene, herein designated VGAM GENE, on one or more VGAM1463 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50769] It is yet further appreciated that a function of VGAM1463 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1463 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1463 correlate with, and may be deduced from, the identity of the host target genes which VGAM1463 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50770] Nucleotide sequences of the VGAM1463 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1463 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1463 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1463 are further described hereinbelow with reference to Table 1.

[50771] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1463 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1463 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50772] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1463 gene, herein designated VGAM is inhibition of expression of VGAM1463 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1463 correlate with, and may be deduced from, the identity of the target genes which VGAM1463 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50773] Death Associated Transcription Factor 1 (DATF1, Accession NM_022105) is a VGAM1463 host target gene. DATF1 BINDING SITE1 and DATF1 BINDING SITE2 are HOST TAR-

GET binding sites found in untranslated regions of mRNA encoded by DATF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DATF1 BINDING SITE1 and DATF1 BINDING SITE2, designated SEQ ID:22650 and SEQ ID:28061 respectively, to the nucleotide sequence of VGAM1463 RNA, herein designated VGAM RNA, also designated SEQ ID:4174.

[50774] A function of VGAM1463 is therefore inhibition of Death Associated Transcription Factor 1 (DATF1, Accession NM_022105). Accordingly, utilities of VGAM1463 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DATF1. KIAA0014 (Accession NM_014665) is another VGAM1463 host target gene. KIAA0014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0014 BINDING SITE, designated SEQ ID:16112, to the nucleotide sequence of VGAM1463 RNA, herein designated VGAM RNA, also designated SEQ

ID:4174.

[50775] Another function of VGAM1463 is therefore inhibition of KIAA0014 (Accession NM_014665). Accordingly, utilities of VGAM1463 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0014. LOC158156 (Accession XM_088496) is another VGAM1463 host target gene. LOC158156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158156 BINDING SITE, designated SEQ ID:39736, to the nucleotide sequence of VGAM1463 RNA, herein designated VGAM RNA, also designated SEQ ID:4174.

[50776] Another function of VGAM1463 is therefore inhibition of LOC158156 (Accession XM_088496). Accordingly, utilities of VGAM1463 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158156. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1464 (VGAM1464) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50777] VGAM1464 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1464 was detected is described hereinabove with reference to Figs. 1–8.

[50778] VGAM1464 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50779] VGAM1464 gene encodes a VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1464 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1464 precursor RNA is designated SEQ ID:1450, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1450 is located at position 42592 relative to the genome of Equine Herpesvirus 2.

[50780] VGAM1464 precursor RNA folds onto itself, forming

VGAM1464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50781] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1464 folded precursor RNA into VGAM1464 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM1464 RNA is designated SEQ ID:4175, and is provided hereinbelow with reference to the sequence listing part.

[50782] VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1464 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50783] VGAM1464 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1464 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1464 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50784] The complementary binding of VGAM1464 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1464 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1464 host target RNA into VGAM1464 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50785] It is appreciated that VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1464 host target genes. The mRNA of each one of this plurality of VGAM1464 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1464 RNA, herein designated VGAM RNA, and which when bound by VGAM1464 RNA causes inhibition of translation of respective one or more VGAM1464 host target proteins.

[50786] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1464 gene, herein designated VGAM GENE, on one or more VGAM1464 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50787] It is yet further appreciated that a function of VGAM1464 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1464 correlate with, and may be deduced from, the identity of the host target genes which VGAM1464 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[50788] Nucleotide sequences of the VGAM1464 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1464 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1464 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1464 are further described hereinbelow with reference to Table 1.

[50789] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1464 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1464 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50790] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1464 gene, herein designated VGAM is inhibition of expression of VGAM1464 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1464 correlate with, and may be deduced from, the identity of the target genes which VGAM1464 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[50791] Citron (rho-interacting, serine/threonine kinase 21) (CIT, Accession XM_045786) is a VGAM1464 host target gene. CIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIT BINDING SITE, designated SEQ ID:34566, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50792] A function of VGAM1464 is therefore inhibition of Citron (rho-interacting, serine/threonine kinase 21) (CIT, Accession XM_045786), a gene which is increased several-fold by coexpression of constitutively active Rho . Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIT. The function of CIT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM393. Death Effector Domain Containing (DEDD, Accession NM_032998) is another VGAM1464 host target gene. DEDD BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by DEDD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEDD BINDING SITE, designated SEQ ID:26880, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50793] Another function of VGAM1464 is therefore inhibition of Death Effector Domain Containing (DEDD, Accession NM_032998), a gene which intervenes in apoptosis. Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEDD. The function of DEDD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM_167853) is another VGAM1464 host target gene. NUMA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NUMA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of NUMA1 BINDING SITE, designated SEQ ID:44882, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50794] Another function of VGAM1464 is therefore inhibition of Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM_167853), a gene which is nuclear mitotic apparatus protein. Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUMA1. The function of NUMA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM192.FLJ10916 (Accession NM_018271) is another VGAM1464 host target gene. FLJ10916 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10916 BINDING SITE, designated SEQ ID:20249, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50795] Another function of VGAM1464 is therefore inhibition of FLJ10916 (Accession NM_018271). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10916. FLJ20584 (Accession NM_017891) is another VGAM1464 host target gene. FLJ20584 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20584 BINDING SITE, designated SEQ ID:19559, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50796] Another function of VGAM1464 is therefore inhibition of FLJ20584 (Accession NM_017891). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20584. KIAA1508 (Accession XM_030209) is another VGAM1464 host target gene. KIAA1508 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1508, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1508 BINDING SITE, designated SEQ ID:30995, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50797] Another function of VGAM1464 is therefore inhibition of KIAA1508 (Accession XM_030209). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1508. MGC2705 (Accession NM_032701) is another VGAM1464 host target gene. MGC2705 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2705 BINDING SITE, designated SEQ ID:26414, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50798] Another function of VGAM1464 is therefore inhibition of MGC2705 (Accession NM_032701). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC2705. Placenta-specific 3 (PLAC3, Accession XM_045115) is another VGAM1464 host target gene. PLAC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAC3 BINDING SITE, designated SEQ ID:34364, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50799] Another function of VGAM1464 is therefore inhibition of Placenta-specific 3 (PLAC3, Accession XM_045115). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAC3. LOC149837 (Accession XM_097747) is another VGAM1464 host target gene. LOC149837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149837 BINDING SITE, desig-

nated SEQ ID:41098, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50800] Another function of VGAM1464 is therefore inhibition of LOC149837 (Accession XM_097747). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149837. LOC51292 (Accession NM_016576) is another VGAM1464 host target gene. LOC51292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51292 BINDING SITE, designated SEQ ID:18652, to the nucleotide sequence of VGAM1464 RNA, herein designated VGAM RNA, also designated SEQ ID:4175.

[50801] Another function of VGAM1464 is therefore inhibition of LOC51292 (Accession NM_016576). Accordingly, utilities of VGAM1464 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51292. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1465 (VGAM1465) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50802] VGAM1465 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1465 was detected is described hereinabove with reference to Figs. 1–8.

[50803] VGAM1465 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50804] VGAM1465 gene encodes a VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1465 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1465 precursor RNA is designated SEQ ID:1451, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1451 is located at position 40669 relative to the

genome of Equine Herpesvirus 2.

[50805] VGAM1465 precursor RNA folds onto itself, forming VGAM1465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50806] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1465 folded precursor RNA into VGAM1465 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1465 RNA is designated SEQ ID:4176, and is provided hereinbelow with reference to the sequence listing part.

[50807] VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1465 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[50808] VGAM1465 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1465 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1465 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[50809] The complementary binding of VGAM1465 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1465 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1465 host target RNA into VGAM1465 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50810] It is appreciated that VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1465 host target genes. The mRNA of each one of this plurality of VGAM1465 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1465 RNA, herein designated VGAM RNA, and which when bound by VGAM1465 RNA causes inhibition of translation of respective one or more VGAM1465 host target proteins.

[50811] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1465 gene, herein designated VGAM GENE, on one or more VGAM1465 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50812] It is yet further appreciated that a function of VGAM1465 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1465

correlate with, and may be deduced from, the identity of the host target genes which VGAM1465 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50813] Nucleotide sequences of the VGAM1465 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1465 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1465 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1465 are further described hereinbelow with reference to Table 1.

[50814] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1465 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1465 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50815] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1465 gene, herein designated VGAM is inhibition of expression of VGAM1465 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1465 correlate with, and may be deduced

from, the identity of the target genes which VGAM1465 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50816] Early Growth Response 2 (Krox-20 homolog, Drosophila) (EGR2, Accession NM_000399) is a VGAM1465 host target gene. EGR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR2 BINDING SITE, designated SEQ ID:5973, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50817] A function of VGAM1465 is therefore inhibition of Early Growth Response 2 (Krox-20 homolog, Drosophila) (EGR2, Accession NM_000399), a gene which binds to two specific dna sites located in the promoter region of hox-1.4. Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR2. The function of EGR2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM234. Inhibin, Beta B

(activin AB beta polypeptide) (INHBB, Accession NM_002193) is another VGAM1465 host target gene. INHBB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INHBB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INHBB BINDING SITE, designated SEQ ID:7948, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50818] Another function of VGAM1465 is therefore inhibition of Inhibin, Beta B (activin AB beta polypeptide) (INHBB, Accession NM_002193), a gene which inhibits inhibit the secretion of follitropin by the pituitary gland. Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INHBB. The function of INHBB has been established by previous studies. The activins, dimers of beta-A or beta-B subunits encoded by the genes *Inhba* (OMIM Ref. No. 147290) and *Inhbb*, respectively, are TGF-beta (see OMIM Ref. No. 190180) superfamily members that have roles in reproduction and development (Brown et al., 2000). Activin ligands act as growth and differentiation

factors in many cells and tissues. Mellor et al. (2000) examined the localization of and dimerization among activin subunits. The results demonstrated that activin beta-C (see OMIM Ref. No. 601233) can form dimers with activin beta-A and beta-B in vitro, but not with the inhibin alpha subunit (OMIM Ref. No. 147380). Using a specific antibody, activin beta-C protein was localized to human liver and prostate and colocalized with beta-A and beta-B subunits to specific cell types in benign and malignant prostate tissues. The capacity to form novel activin heterodimers (but not inhibin C) appears to reside in the human liver and prostate. The authors concluded that formation of activin AC or BC heterodimers may have significant implications in the regulation of levels and/or biologic activity of other activins in these tissues. Malignancy of pheochromocytomas is difficult to estimate on the basis of histopathologic features. In a search for new markers to differentiate malignant pheochromocytomas from benign ones, Salmenkivi et al. (2001) tested the value of inhibin/activin subunit expression. Inhibins are heterodimeric glycoproteins consisting of an alpha subunit and either a beta-A or a beta-B subunit. Activins are composed of beta subunits only. Immunohistochemically, in-

hibin/activin beta-B subunit was strongly positive in the normal adrenal medulla, but the cortex was negative. A striking difference was found in inhibin/activin beta-B expression between benign and malignant pheochromocytomas. The majority of benign adrenal tumors (27 of 30) showed strong or moderate immunoreactivity, whereas all 7 malignant tumors were negative or only weakly positive for inhibin/activin beta-B subunit. Salmenkivi et al. (2001) suggested that inhibin/activin beta-B subunit is expressed in normal adrenal medullary cells. Strong staining was found in most benign adrenal pheochromocytomas, whereas malignant tumors were almost negative. They concluded that loss of inhibin/activin beta-B subunit expression in pheochromocytomas may be used as an indicator of malignant potential. Animal model experiments lend further support to the function of INHBB. Whereas mice homozygous for the *Inhba*-null allele demonstrate disruption of whisker, palate, and tooth development leading to neonatal lethality, homozygous *Inhbb*-null mice are viable, fertile, and have eye defects. To determine if these phenotypes were due to spatiotemporal expression differences of the ligands or disruption of specific ligand-receptor interactions, Brown et al. (2000) replaced the re-

gion of *Inhba* encoding the mature protein with *Inhbb*, creating the allele designated *Inhba*(BK). Although the craniofacial phenotypes of the *Inhba*-null mutation were rescued by the *Inhba*(BK) allele, somatic, testicular, genital, and hair growth were grossly affected and influenced by the dosage and bioactivity of the allele. Thus, Brown et al. (2000) concluded that functional compensation within the TGF- β superfamily can occur if the replacement gene is expressed appropriately. The novel phenotypes in these mice further illustrate the usefulness of insertion strategies for defining protein function. The structural organization of the testes of adult *Inhba*(BK/BK) mice was normal; however, the differentiation of the seminiferous tubules of *Inhba*(BK/-) mice was delayed. The testicular volumes of both *Inhba*(BK/BK) and *Inhba*(BK/-) mice were less than those of controls, and the dosage of the *Inhba*(BK) allele correlated positively with testicular size. *Inhba*(+/BK) males had normal onset of fertility, whereas *Inhba*(BK/BK) males had delayed onset of fertility similar to *Acvr2* (OMIM Ref. No. 102581) -/- mice. Only 1 in 6 *Inhba*(BK/BK) females produced litters, whereas *Inhba*(+/BK) females were normally fertile. The ovaries of *Inhba*(BK/-) mice were smaller and contained fewer large preantral

follicles than those of controls. Inhba(BK/BK) and Inhba(BK/–) mice were identified by their smaller size, slower hair growth, the rough appearance of their fur, and sunken eyes. Approximately 50% of Inhba(BK/BK) mice died by 26 weeks, whereas Inhba(BK/–) mice invariably became cachectic and died between 3 and 4 weeks. The summary of phenotypic findings of Inhba(BK/–) mice includes short whiskers, normal tooth development, no cleft palate, symmetric growth deficiency (OMIM Ref. No. severe), enlargement of external genitalia, hypogonadism (OMIM Ref. No. severe), delayed hair growth (moderate), hypoglycemia (mild), decreased life expectancy (OMIM Ref. No. severe), and anemia

[50819] It is appreciated that the abovementioned animal model for INHBB is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[50820] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50821] Salmenkivi, K.; Arola, J.; Voutilainen, R.; Ilvesmaki, V.; Haglund, C.; Kahri, A. I.; Heikkila, P.; Liu, J. : Inhibin/activin beta-B-subunit expression in pheochromocytomas

favours benign diagnosis. J. Clin. Endocr. Metab. 86: 2231–2235, 2001. ; and

[50822] Brown, C. W.; Houston–Hawkins, D. E.; Woodruff, T. K.; Matzuk, M. M. : Insertion of Inhbb into the Inhba locus rescues the Inhba–null phenotype and reveals new activin functions. Nature.

[50823] Further studies establishing the function and utilities of INHBB are found in John Hopkins OMIM database record ID 147390, and in cited publications numbered 5241, 11328–524 and 11329–11330 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM_002570) is another VGAM1465 host target gene. PACE4 BINDING SITE1 and PACE4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PACE4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE4 BINDING SITE1 and PACE4 BINDING SITE2, designated SEQ ID:8432 and SEQ ID:28721 respectively, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50824] Another function of VGAM1465 is therefore inhibition of Paired Basic Amino Acid Cleaving System 4 (PACE4, Accession NM_002570), a gene which processes hormone precursors by cleaving paired basic amino acids. Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE4. The function of PACE4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1194. Potassium Voltage-gated Channel, Delayed-rectifier, Subfamily S, Member 1 (KCNS1, Accession NM_002251) is another VGAM1465 host target gene. KCNS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS1 BINDING SITE, designated SEQ ID:8048, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50825] Another function of VGAM1465 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Sub-

family S, Member 1 (KCNS1, Accession NM_002251). Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS1. KIAA1045 (Accession XM_048592) is another VGAM1465 host target gene. KIAA1045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35195, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50826] Another function of VGAM1465 is therefore inhibition of KIAA1045 (Accession XM_048592). Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1045. LOC152195 (Accession XM_098172) is another VGAM1465 host target gene. LOC152195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC152195 BINDING SITE, designated SEQ ID:41434, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50827] Another function of VGAM1465 is therefore inhibition of LOC152195 (Accession XM_098172). Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152195. LOC199990 (Accession XM_114083) is another VGAM1465 host target gene. LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42685, to the nucleotide sequence of VGAM1465 RNA, herein designated VGAM RNA, also designated SEQ ID:4176.

[50828] Another function of VGAM1465 is therefore inhibition of LOC199990 (Accession XM_114083). Accordingly, utilities of VGAM1465 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1466 (VGAM1466) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50829] VGAM1466 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1466 was detected is described hereinabove with reference to Figs. 1–8.

[50830] VGAM1466 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50831] VGAM1466 gene encodes a VGAM1466 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1466 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1466 precursor RNA is designated SEQ ID:1452, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1452 is located at position 39035 relative to the genome of Equine Herpesvirus 2.

[50832] VGAM1466 precursor RNA folds onto itself, forming VGAM1466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50833] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1466 folded precursor RNA into VGAM1466 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1466 RNA is designated SEQ ID:4177, and is provided hereinbelow with reference to the sequence listing part.

[50834] VGAM1466 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1466 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50835] VGAM1466 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1466 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1466 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1466 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[50836] The complementary binding of VGAM1466 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1466 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1466 host target RNA into VGAM1466 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50837] It is appreciated that VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1466 host target genes. The mRNA of each one of this plurality of VGAM1466 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1466 RNA, herein designated VGAM RNA, and which when bound by VGAM1466 RNA causes inhibition of translation of respective one or more

VGAM1466 host target proteins.

[50838] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1466 gene, herein designated VGAM GENE, on one or more VGAM1466 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50839] It is yet further appreciated that a function of VGAM1466 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Spe-

cific functions, and accordingly utilities, of VGAM1466 correlate with, and may be deduced from, the identity of the host target genes which VGAM1466 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50840] Nucleotide sequences of the VGAM1466 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1466 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1466 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1466 are further described hereinbelow with reference to Table 1.

[50841] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1466 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1466 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[50842] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1466 gene, herein designated VGAM is inhibition of expression of VGAM1466 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1466 correlate with, and may be deduced from, the identity of the target genes which VGAM1466 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[50843] Adenylate Cyclase 6 (ADCY6, Accession NM_015270) is a VGAM1466 host target gene. ADCY6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADCY6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE, designated SEQ ID:17593, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50844] A function of VGAM1466 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM_015270), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY6. The function of ADCY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM22.B-cell CLL/lymphoma 10 (BCL10, Accession NM_003921) is another VGAM1466 host target gene. BCL10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL10 BINDING SITE, designated SEQ ID:10010, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50845] Another function of VGAM1466 is therefore inhibition of B-cell CLL/lymphoma 10 (BCL10, Accession NM_003921), a gene which is a positive regulator of lymphocyte proliferation, NF-kappaB activator. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL10. The function of BCL10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433.Caspase Recruitment Domain Family, Member 15 (CARD15, Accession NM_022162) is another VGAM1466 host target gene. CARD15 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD15 BINDING SITE, designated SEQ ID:22720, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50846] Another function of VGAM1466 is therefore inhibition of Caspase Recruitment Domain Family, Member 15 (CARD15, Accession NM_022162), a gene which serves as an intracellular receptor for bacterial products in monocytes and transduces signals leading to NFkB activation. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARD15. The function of CARD15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM126.CDC6 Cell Division Cycle 6 Homolog (*S. cerevisiae*) (CDC6, Accession NM_001254) is another VGAM1466 host target gene. CDC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

CDC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC6 BINDING SITE, designated SEQ ID:6924, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50847] Another function of VGAM1466 is therefore inhibition of CDC6 Cell Division Cycle 6 Homolog (*S. cerevisiae*) (CDC6, Accession NM_001254), a gene which is a component of the origin recognition complex (orc) that binds origins of replication. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC6. The function of CDC6 has been established by previous studies. In yeasts, Cdc6 (*Saccharomyces cerevisiae*) and Cdc18 (*Schizosaccharomyces pombe*) associate with the origin recognition complex (ORC) proteins to render cells competent for DNA replication. Thus, Cdc6 has a critical regulatory role in the initiation of DNA replication in yeast. Williams et al. (1997) isolated cDNAs encoding *Xenopus* and human homologs of yeast CDC6. They designated the human and *Xenopus* proteins p62(cdc6). Independently, in a yeast 2-hybrid assay using PCNA (OMIM Ref. No.

176740) as bait, Saha et al. (1998) isolated cDNAs encoding the human CDC6/Cdc18 homolog. These authors reported that the predicted 560-amino acid human protein shares approximately 33% sequence identity with the 2 yeast proteins. On Western blots of HeLa cell extracts, human CDC6/cdc18 migrates as a 66-kD protein. Although Northern blots indicated that CDC6/Cdc18 mRNA levels peak at the onset of S phase and diminish at the onset of mitosis in HeLa cells, the authors found that total CDC6/Cdc18 protein level is unchanged throughout the cell cycle. Immunofluorescent analysis of epitope-tagged protein revealed that human CDC6/Cdc18 is nuclear in G1- and cytoplasmic in S-phase cells, suggesting that DNA replication may be regulated by either the translocation of this protein between the nucleus and cytoplasm or by selective degradation of the protein in the nucleus. Immunoprecipitation studies showed that human CDC6/Cdc18 associates in vivo with cyclin A (OMIM Ref. No. 123835), CDK2 (OMIM Ref. No. 116953), and ORC1 (OMIM Ref. No. 601902). The association of cyclin-CDK2 with CDC6/Cdc18 was specifically inhibited by a factor present in mitotic cell extracts. Saha et al. (1998) suggested that if the interaction between CDC6/Cdc18 with

the S phase–promoting factor cyclin–CDK2 is essential for the initiation of DNA replication, the mitotic inhibitor of this interaction could prevent a premature interaction until the appropriate time in G1.

[50848] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50849] Williams, R. S.; Shohet, R. V.; Stillman, B. : A human protein related to yeast Cdc6p. Proc. Nat. Acad. Sci. 94: 142–147, 1997. ; and

[50850] Saha, P.; Chen, J.; Thome, K. C.; Lawlis, S. J.; Hou, Z.–H.; Hendricks, M.; Parvin, J. D.; Dutta, A. : Human CDC6/Cdc18 associates with Orc1 and cyclin–cdk and is selectively eliminated.

[50851] Further studies establishing the function and utilities of CDC6 are found in John Hopkins OMIM database record ID 602627, and in cited publications numbered 8565–856 and 9449 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cadherin 17, LI Cadherin (liver–intestine) (CDH17, Accession NM_004063) is another VGAM1466 host target gene. CDH17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

CDH17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH17 BINDING SITE, designated SEQ ID:10271, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50852] Another function of VGAM1466 is therefore inhibition of Cadherin 17, LI Cadherin (liver–intestine) (CDH17, Accession NM_004063), a gene which may have a role in the morphological organization of liver and intestine and involved in intestinal peptide transport. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH17. The function of CDH17 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Cholinergic Receptor, Muscarinic 1 (CHRM1, Accession XM_170669) is another VGAM1466 host target gene. CHRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRM1 BINDING SITE, designated SEQ ID:45442, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50853] Another function of VGAM1466 is therefore inhibition of Cholinergic Receptor, Muscarinic 1 (CHRM1, Accession XM_170669), a gene which mediates various cellular responses. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRM1. The function of CHRM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM302.COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_078470) is another VGAM1466 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:27792, to the

nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50854] Another function of VGAM1466 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_078470). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052) is another VGAM1466 host target gene. DSCR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR3 BINDING SITE, designated SEQ ID:12689, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50855] Another function of VGAM1466 is therefore inhibition of Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR3. Fibulin 5 (FBLN5,

Accession NM_006329) is another VGAM1466 host target gene. FBLN5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBLN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBLN5 BINDING SITE, designated SEQ ID:13025, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50856] Another function of VGAM1466 is therefore inhibition of Fibulin 5 (FBLN5, Accession NM_006329), a gene which promotes adhesion of endothelial cells through interaction of integrins and the rgd motif. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBLN5. The function of FBLN5 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1127. Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is another VGAM1466 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14883, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50857] Another function of VGAM1466 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.GNE (Accession NM_005476) is another VGAM1466 host target gene. GNE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

GNE BINDING SITE, designated SEQ ID:11977, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50858] Another function of VGAM1466 is therefore inhibition of GNE (Accession NM_005476), a gene which has roles in sialic acid biosynthesis and regulates cell surface sialylation. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNE. The function of GNE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM362.GRAF (Accession NM_015071) is another VGAM1466 host target gene. GRAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRAF BINDING SITE, designated SEQ ID:17444, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50859] Another function of VGAM1466 is therefore inhibition of GRAF (Accession NM_015071), a gene which is a GTPase

activating protein for p21–rac. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRAF. The function of GRAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM430. Glutamate Receptor, Ionotropic, Kainate 3 (GRIK3, Accession NM_000831) is another VGAM1466 host target gene. GRIK3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GRIK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIK3 BINDING SITE, designated SEQ ID:6487, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50860] Another function of VGAM1466 is therefore inhibition of Glutamate Receptor, Ionotropic, Kainate 3 (GRIK3, Accession NM_000831). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIK3. Kinesin Heavy Chain Member 2 (KIF2, Accession NM_004520) is another

VGAM1466 host target gene. KIF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF2 BINDING SITE, designated SEQ ID:10849, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50861] Another function of VGAM1466 is therefore inhibition of Kinesin Heavy Chain Member 2 (KIF2, Accession NM_004520). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF2. LENG4 (Accession NM_024298) is another VGAM1466 host target gene. LENG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LENG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23588, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ

ID:4177.

[50862] Another function of VGAM1466 is therefore inhibition of LENG4 (Accession NM_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM259.V-myb Myeloblastosis Viral Oncogene Homolog (avian) (MYB, Accession XM_004256) is another VGAM1466 host target gene. MYB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYB BINDING SITE, designated SEQ ID:29944, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50863] Another function of VGAM1466 is therefore inhibition of V-myb Myeloblastosis Viral Oncogene Homolog (avian) (MYB, Accession XM_004256). Accordingly, utilities of

VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYB. Neurocalcin Delta (NCALD, Accession NM_032041) is another VGAM1466 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25747, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50864] Another function of VGAM1466 is therefore inhibition of Neurocalcin Delta (NCALD, Accession NM_032041). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. Protocadherin Alpha 9 (PCDHA9, Accession NM_014005) is another VGAM1466 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PCDHA9 BINDING SITE, designated SEQ ID:15213, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50865] Another function of VGAM1466 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_014005), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is another VGAM1466 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12886, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM

RNA, also designated SEQ ID:4177.

[50866] Another function of VGAM1466 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117. Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768) is another VGAM1466 host target gene. PEA15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEA15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEA15 BINDING SITE, designated SEQ ID:9853, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50867] Another function of VGAM1466 is therefore inhibition of

Phosphoprotein Enriched In Astrocytes 15 (PEA15, Accession NM_003768), a gene which is a phosphoprotein and involved in glucose uptake. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEA15. The function of PEA15 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM949. Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM_043865) is another VGAM1466 host target gene. PIK3R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R1 BINDING SITE, designated SEQ ID:34038, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50868] Another function of VGAM1466 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 1 (p85 alpha) (PIK3R1, Accession XM_043865), a gene

which acts as an adapter, for the insulin-stimulated increase in glucose uptake and glycogen synthesis. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R1. The function of PIK3R1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM826. Protein Phosphatase, EF Hand Calcium-binding Domain 2 (PPEF2, Accession NM_006239) is another VGAM1466 host target gene. PPEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPEF2 BINDING SITE, designated SEQ ID:12905, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50869] Another function of VGAM1466 is therefore inhibition of Protein Phosphatase, EF Hand Calcium-binding Domain 2 (PPEF2, Accession NM_006239), a gene which is a homolog of *Drosophila* rdgC. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with PPEF2. The function of PPEF2 has been established by previous studies. During random sequencing of human retina cDNAs, Sherman et al. (1997) identified a homolog of *Drosophila* rdgC. Full-length cDNAs of the gene, termed PPEF2, predicted a 753-amino acid protein that is 39% identical to that of *Drosophila* rdgC and has a domain structure similar to that of rdgC and PPEF1 (OMIM Ref. No. 300109). Sherman et al. (1997) noted the existence of a shorter alternatively spliced form of PPEF2, termed PPEF2(S), that uses alternative splice acceptor sites in exons 5 and 14 and predicts a 598-amino acid protein lacking EF-hand domains. Northern blot analysis of rat tissues revealed a 3.7-kb PPEF2 mRNA in retina. In situ hybridization and cell fractionation experiments further revealed that the gene is expressed exclusively in the inner segments of the photoreceptor cells of the retina and in the pineal gland. Sherman et al. (1997) stated that the inner segment localization implies that PPEF2 probably does not dephosphorylate rhodopsin and is probably not directly involved in phototransduction. Animal model experiments lend further support to the function of PPEF2. Ramulu et al. (2001) produced mice carrying targeted disruptions in

the Ppef1 and Ppef2 genes. By analyzing both single and double mutant mice, they observed that rod light responses and rhodopsin dephosphorylation kinetics were normal. Furthermore, there was no evidence of retinal degeneration in the PPEF mutant mice. Ramulu et al. (2001) concluded that in contrast to loss of rdgC function in *Drosophila*, elimination of PPEF function does not cause retinal degeneration in vertebrates.

[50870] It is appreciated that the abovementioned animal model for PPEF2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[50871] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[50872] Ramulu, P.; Kennedy, M.; Xiong, W.-H.; Williams, J.; Cowan, M.; Blesh, D.; Yau, K.-W.; Hurley, J. B.; Nathans, J. : Normal light response, photoreceptor integrity, and rhodopsin dephosphorylation in mice lacking both protein phosphatases with EF hands (PPEF-1 and PPEF-2). *Molec. Cell. Biol.* 21: 8605-8614, 2001. ; and

[50873] Sherman, P. M.; Sun, H.; Macke, J. P.; Williams, J.; Smallwood, P. M.; Nathans, J. : Identification and characteriza-

tion of a conserved family of protein serine/threonine phosphatases h.

[50874] Further studies establishing the function and utilities of PPEF2 are found in John Hopkins OMIM database record ID 602256, and in cited publications numbered 10627 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rabphilin 3A-like (without C2 domains) (RPH3AL, Accession NM_006987) is another VGAM1466 host target gene. RPH3AL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPH3AL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPH3AL BINDING SITE, designated SEQ ID:13849, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50875] Another function of VGAM1466 is therefore inhibition of Rabphilin 3A-like (without C2 domains) (RPH3AL, Accession NM_006987), a gene which is a protein transporter. could play a role in neurotransmitter release by regulating membrane flow in the nerve terminal. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with RPH3AL. The function of RPH3AL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM1466 host target gene. SEDL BINDING SITE1 and SEDL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEDL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEDL BINDING SITE1 and SEDL BINDING SITE2, designated SEQ ID:15915 and SEQ ID:15916 respectively, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50876] Another function of VGAM1466 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association

with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM_144585) is another VGAM1466 host target gene. SLC22A12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC22A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC22A12 BINDING SITE, designated SEQ ID:29405, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50877] Another function of VGAM1466 is therefore inhibition of Solute Carrier Family 22 (organic anion/cation transporter), Member 12 (SLC22A12, Accession NM_144585), a gene which is a urate -anion exchanger regulating blood urate levels. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC22A12. The function of SLC22A12 and its association with various diseases and clinical conditions, has been established by previous stud-

ies, as described hereinabove with reference to VGAM1034. Thromboxane A2 Receptor (TBXA2R, Accession NM_001060) is another VGAM1466 host target gene. TBXA2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBXA2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBXA2R BINDING SITE, designated SEQ ID:6731, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50878] Another function of VGAM1466 is therefore inhibition of Thromboxane A2 Receptor (TBXA2R, Accession NM_001060), a gene which activates Ca²⁺-activated chloride channels; stimulates platelet aggregation and smooth muscle constriction. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBXA2R. The function of TBXA2R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM433. Tec Protein Tyrosine Kinase (TEC,

Accession NM_003215) is another VGAM1466 host target gene. TEC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEC BINDING SITE, designated SEQ ID:9219, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50879] Another function of VGAM1466 is therefore inhibition of Tec Protein Tyrosine Kinase (TEC, Accession NM_003215). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEC. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM1466 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15357, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4177.

[50880] Another function of VGAM1466 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Ubiquitin Specific Protease 9, Y Chromosome (fat facets-like Drosophila) (USP9Y, Accession XM_034147) is another VGAM1466 host target gene. USP9Y BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP9Y, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP9Y BINDING SITE, designated SEQ ID:32018, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50881] Another function of VGAM1466 is therefore inhibition of

Ubiquitin Specific Protease 9, Y Chromosome (fat facets-like *Drosophila*) (USP9Y, Accession XM_034147), a gene which removes ubiquitin from ubiquitin-conjugated proteins and has a role in spermatogenesis. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP9Y. The function of USP9Y and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM894. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919) is another VGAM1466 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:17185, SEQ ID:28449 and SEQ ID:28466 respectively, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50882] Another function of VGAM1466 is therefore inhibition of

Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM_019034) is another VGAM1466 host target gene. ARHF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHF BINDING SITE, designated SEQ ID:21122, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50883] Another function of VGAM1466 is therefore inhibition of Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM_019034). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with ARHF. ARPP-19 (Accession NM_006628) is another VGAM1466 host target gene. ARPP-19 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARPP-19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARPP-19 BINDING SITE, designated SEQ ID:13425, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50884] Another function of VGAM1466 is therefore inhibition of ARPP-19 (Accession NM_006628). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARPP-19. Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418) is another VGAM1466 host target gene. C11orf25 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C11orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf25 BINDING SITE, designated

SEQ ID:25401, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50885] Another function of VGAM1466 is therefore inhibition of Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf25. C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM_031910) is another VGAM1466 host target gene. C1QTNF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF6 BINDING SITE, designated SEQ ID:25660, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50886] Another function of VGAM1466 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM_031910). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with C1QTNF6. Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956) is another VGAM1466 host target gene. C9orf9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C9orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf9 BINDING SITE, designated SEQ ID:21030, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50887] Another function of VGAM1466 is therefore inhibition of Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf9. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM1466 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25520, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50888] Another function of VGAM1466 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. Caspase Recruitment Domain Family, Member 6 (CARD6, Accession NM_032587) is another VGAM1466 host target gene. CARD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARD6 BINDING SITE, designated SEQ ID:26323, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50889] Another function of VGAM1466 is therefore inhibition of Caspase Recruitment Domain Family, Member 6 (CARD6, Accession NM_032587). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with CARD6. Chromobox Homolog 6 (CBX6, Accession NM_014292) is another VGAM1466 host target gene. CBX6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CBX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX6 BINDING SITE, designated SEQ ID:15579, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50890] Another function of VGAM1466 is therefore inhibition of Chromobox Homolog 6 (CBX6, Accession NM_014292). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX6. CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM_003672) is another VGAM1466 host target gene. CDC14A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDC14A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CDC14A BINDING SITE, designated SEQ ID:9766, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50891] Another function of VGAM1466 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog A (*S. cerevisiae*) (CDC14A, Accession NM_003672). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14A. Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444) is another VGAM1466 host target gene. CHRAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRAC1 BINDING SITE, designated SEQ ID:18906, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50892] Another function of VGAM1466 is therefore inhibition of Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444). Accordingly, utilities of VGAM1466 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRAC1. DKFZP434F0318 (Accession NM_030817) is another VGAM1466 host target gene. DKFZP434F0318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434F0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F0318 BINDING SITE, designated SEQ ID:25144, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50893] Another function of VGAM1466 is therefore inhibition of DKFZP434F0318 (Accession NM_030817). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F0318. DKFZP564G092 (Accession NM_015601) is another VGAM1466 host target gene. DKFZP564G092 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564G092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of DKFZP564G092 BINDING SITE, designated SEQ ID:17878, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50894] Another function of VGAM1466 is therefore inhibition of DKFZP564G092 (Accession NM_015601). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564G092. DKFZP564O0463 (Accession NM_014156) is another VGAM1466 host target gene. DKFZP564O0463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0463 BINDING SITE, designated SEQ ID:15446, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50895] Another function of VGAM1466 is therefore inhibition of DKFZP564O0463 (Accession NM_014156). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP564O0463. DKFZp761O0113 (Accession NM_018409) is another VGAM1466 host target gene. DKFZp761O0113 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761O0113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761O0113 BINDING SITE, designated SEQ ID:20449, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50896] Another function of VGAM1466 is therefore inhibition of DKFZp761O0113 (Accession NM_018409). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761O0113. Eukaryotic Translation Initiation Factor 2C, 2 (EIF2C2, Accession XM_050334) is another VGAM1466 host target gene. EIF2C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C2 BIND-

ING SITE, designated SEQ ID:35614, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50897] Another function of VGAM1466 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 2 (EIF2C2, Accession XM_050334). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2C2. FLJ12903 (Accession NM_022753) is another VGAM1466 host target gene. FLJ12903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12903 BINDING SITE, designated SEQ ID:22984, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50898] Another function of VGAM1466 is therefore inhibition of FLJ12903 (Accession NM_022753). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12903. FLJ13188 (Accession NM_022063) is another

VGAM1466 host target gene. FLJ13188 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13188, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13188 BINDING SITE, designated SEQ ID:22607, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50899] Another function of VGAM1466 is therefore inhibition of FLJ13188 (Accession NM_022063). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13188. FLJ13197 (Accession NM_024614) is another VGAM1466 host target gene. FLJ13197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13197 BINDING SITE, designated SEQ ID:23875, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50900] Another function of VGAM1466 is therefore inhibition of FLJ13197 (Accession NM_024614). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13197. FLJ14084 (Accession NM_021637) is another VGAM1466 host target gene. FLJ14084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14084 BINDING SITE, designated SEQ ID:22285, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50901] Another function of VGAM1466 is therefore inhibition of FLJ14084 (Accession NM_021637). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14084. FLJ14950 (Accession NM_032865) is another VGAM1466 host target gene. FLJ14950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14950 BINDING SITE, designated SEQ ID:26678, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50902] Another function of VGAM1466 is therefore inhibition of FLJ14950 (Accession NM_032865). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14950. FLJ14957 (Accession NM_032866) is another VGAM1466 host target gene. FLJ14957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14957 BINDING SITE, designated SEQ ID:26685, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50903] Another function of VGAM1466 is therefore inhibition of FLJ14957 (Accession NM_032866). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ14957. FLJ20010 (Accession NM_019021) is another VGAM1466 host target gene. FLJ20010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20010 BINDING SITE, designated SEQ ID:21110, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50904] Another function of VGAM1466 is therefore inhibition of FLJ20010 (Accession NM_019021). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20010. FLJ20695 (Accession NM_017929) is another VGAM1466 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20695, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19615, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM

RNA, also designated SEQ ID:4177.

[50905] Another function of VGAM1466 is therefore inhibition of FLJ20695 (Accession NM_017929). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. FLJ22944 (Accession NM_025145) is another VGAM1466 host target gene. FLJ22944 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22944 BINDING SITE, designated SEQ ID:24784, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50906] Another function of VGAM1466 is therefore inhibition of FLJ22944 (Accession NM_025145). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22944. FLJ23519 (Accession NM_032240) is another VGAM1466 host target gene. FLJ23519 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23519, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23519 BINDING SITE, designated SEQ ID:25978, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50907] Another function of VGAM1466 is therefore inhibition of FLJ23519 (Accession NM_032240). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23519. FLJ31101 (Accession NM_017964) is another VGAM1466 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19687, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50908] Another function of VGAM1466 is therefore inhibition of FLJ31101 (Accession NM_017964). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ31101. FLJ31153 (Accession NM_144600) is another VGAM1466 host target gene. FLJ31153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31153 BINDING SITE, designated SEQ ID:29415, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50909] Another function of VGAM1466 is therefore inhibition of FLJ31153 (Accession NM_144600). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31153. GREB1 (Accession NM_014668) is another VGAM1466 host target gene. GREB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GREB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GREB1 BINDING SITE, designated SEQ ID:16126, to the nucleotide sequence of

VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50910] Another function of VGAM1466 is therefore inhibition of GREB1 (Accession NM_014668). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GREB1. GRP3 (Accession NM_015376) is another VGAM1466 host target gene. GRP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRP3 BINDING SITE, designated SEQ ID:17674, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50911] Another function of VGAM1466 is therefore inhibition of GRP3 (Accession NM_015376). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRP3. HSMPP8 (Accession XM_167894) is another VGAM1466 host target gene. HSMPP8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by HSMPP8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSMPP8 BINDING SITE, designated SEQ ID:44905, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50912] Another function of VGAM1466 is therefore inhibition of HSMPP8 (Accession XM_167894). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSMPP8. JM11 (Accession NM_033626) is another VGAM1466 host target gene. JM11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JM11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JM11 BINDING SITE, designated SEQ ID:27333, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50913] Another function of VGAM1466 is therefore inhibition of JM11 (Accession NM_033626). Accordingly, utilities of

VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JM11. KIAA0087 (Accession NM_014769) is another VGAM1466 host target gene. KIAA0087 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0087 BINDING SITE, designated SEQ ID:16561, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50914] Another function of VGAM1466 is therefore inhibition of KIAA0087 (Accession NM_014769). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0087. KIAA0352 (Accession NM_014830) is another VGAM1466 host target gene. KIAA0352 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0352 BINDING SITE, designated SEQ ID:16826, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50915] Another function of VGAM1466 is therefore inhibition of KIAA0352 (Accession NM_014830). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0352. KIAA0449 (Accession NM_017596) is another VGAM1466 host target gene. KIAA0449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0449 BINDING SITE, designated SEQ ID:19054, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50916] Another function of VGAM1466 is therefore inhibition of KIAA0449 (Accession NM_017596). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0449. KIAA0472 (Accession XM_050147) is another VGAM1466 host target gene. KIAA0472 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0472, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0472 BINDING SITE, designated SEQ ID:35584, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50917] Another function of VGAM1466 is therefore inhibition of KIAA0472 (Accession XM_050147). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0472. KIAA0513 (Accession NM_014732) is another VGAM1466 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16364, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50918] Another function of VGAM1466 is therefore inhibition of

KIAA0513 (Accession NM_014732). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. KIAA0557 (Accession XM_085507) is another VGAM1466 host target gene. KIAA0557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0557 BINDING SITE, designated SEQ ID:38213, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50919] Another function of VGAM1466 is therefore inhibition of KIAA0557 (Accession XM_085507). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0557. KIAA0828 (Accession XM_088105) is another VGAM1466 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39516, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50920] Another function of VGAM1466 is therefore inhibition of KIAA0828 (Accession XM_088105). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. KIAA0831 (Accession NM_014924) is another VGAM1466 host target gene. KIAA0831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0831 BINDING SITE, designated SEQ ID:17210, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50921] Another function of VGAM1466 is therefore inhibition of KIAA0831 (Accession NM_014924). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0831. KIAA1198 (Accession XM_032674) is another

VGAM1466 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31719, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50922] Another function of VGAM1466 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1257 (Accession XM_031577) is another VGAM1466 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31443, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50923] Another function of VGAM1466 is therefore inhibition of KIAA1257 (Accession XM_031577). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. KIAA1430 (Accession XM_087593) is another VGAM1466 host target gene. KIAA1430 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1430 BINDING SITE, designated SEQ ID:39358, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50924] Another function of VGAM1466 is therefore inhibition of KIAA1430 (Accession XM_087593). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1430. KIAA1500 (Accession XM_034353) is another VGAM1466 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32070, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50925] Another function of VGAM1466 is therefore inhibition of KIAA1500 (Accession XM_034353). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1500. KIAA1655 (Accession XM_039442) is another VGAM1466 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33092, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50926] Another function of VGAM1466 is therefore inhibition of KIAA1655 (Accession XM_039442). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1655. KIAA1727 (Accession XM_034262) is another VGAM1466 host target gene. KIAA1727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1727 BINDING SITE, designated SEQ ID:32037, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50927] Another function of VGAM1466 is therefore inhibition of KIAA1727 (Accession XM_034262). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1727. KIAA1971 (Accession XM_058720) is another VGAM1466 host target gene. KIAA1971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1971 BINDING SITE, designated SEQ ID:36732, to the nucleotide sequence of VGAM1466 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4177.

[50928] Another function of VGAM1466 is therefore inhibition of KIAA1971 (Accession XM_058720). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1971. Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277) is another VGAM1466 host target gene. KLK7 BINDING SITE1 and KLK7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KLK7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLK7 BINDING SITE1 and KLK7 BINDING SITE2, designated SEQ ID:29275 and SEQ ID:11478 respectively, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50929] Another function of VGAM1466 is therefore inhibition of Kallikrein 7 (chymotryptic, stratum corneum) (KLK7, Accession NM_139277). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLK7. MGC21675 (Accession NM_052861) is another VGAM1466 host target

gene. MGC21675 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC21675, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21675 BINDING SITE, designated SEQ ID:27446, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50930] Another function of VGAM1466 is therefore inhibition of MGC21675 (Accession NM_052861). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21675. MGC4707 (Accession NM_024113) is another VGAM1466 host target gene. MGC4707 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4707 BINDING SITE, designated SEQ ID:23565, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50931] Another function of VGAM1466 is therefore inhibition of MGC4707 (Accession NM_024113). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4707. Ninjurin 2 (NINJ2, Accession NM_016533) is another VGAM1466 host target gene. NINJ2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NINJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NINJ2 BINDING SITE, designated SEQ ID:18606, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50932] Another function of VGAM1466 is therefore inhibition of Ninjurin 2 (NINJ2, Accession NM_016533). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NINJ2. Nup43 (Accession NM_024647) is another VGAM1466 host target gene. Nup43 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by Nup43, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Nup43 BINDING SITE, designated SEQ ID:23938, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50933] Another function of VGAM1466 is therefore inhibition of Nup43 (Accession NM_024647). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Nup43. OCT11 (Accession NM_014352) is another VGAM1466 host target gene. OCT11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OCT11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCT11 BINDING SITE, designated SEQ ID:15680, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50934] Another function of VGAM1466 is therefore inhibition of OCT11 (Accession NM_014352). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCT11.

PAI-RBP1 (Accession NM_015640) is another VGAM1466 host target gene. PAI-RBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PAI-RBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAI-RBP1 BINDING SITE, designated SEQ ID:17894, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50935] Another function of VGAM1466 is therefore inhibition of PAI-RBP1 (Accession NM_015640). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAI-RBP1. Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651) is another VGAM1466 host target gene. PELI1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PELI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI1 BINDING SITE, designated SEQ ID:21818, to the nucleotide sequence of VGAM1466 RNA, herein

designated VGAM RNA, also designated SEQ ID:4177.

[50936] Another function of VGAM1466 is therefore inhibition of Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI1. PIP3-E (Accession XM_039749) is another VGAM1466 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33181, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50937] Another function of VGAM1466 is therefore inhibition of PIP3-E (Accession XM_039749). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM_024607) is another VGAM1466 host target gene. PPP1R3B BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by PPP1R3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R3B BINDING SITE, designated SEQ ID:23858, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50938] Another function of VGAM1466 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 3B (PPP1R3B, Accession NM_024607). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R3B. PRO2198 (Accession NM_018621) is another VGAM1466 host target gene. PRO2198 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO2198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2198 BINDING SITE, designated SEQ ID:20695, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50939] Another function of VGAM1466 is therefore inhibition of PRO2198 (Accession NM_018621). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2198. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737) is another VGAM1466 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16398, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50940] Another function of VGAM1466 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. RGPR (Accession NM_033127) is another VGAM1466 host target gene. RGPR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by RGPR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGPR BINDING SITE, designated SEQ ID:26971, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50941] Another function of VGAM1466 is therefore inhibition of RGPR (Accession NM_033127). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGPR. SCYA22 (Accession XM_165651) is another VGAM1466 host target gene. SCYA22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYA22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYA22 BINDING SITE, designated SEQ ID:43717, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50942] Another function of VGAM1466 is therefore inhibition of SCYA22 (Accession XM_165651). Accordingly, utilities of

VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYA22. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263) is another VGAM1466 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10461, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50943] Another function of VGAM1466 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. Solute Carrier Family 6 (neurotransmitter transporter), Member 14 (SLC6A14, Accession NM_007231) is another VGAM1466 host target

gene. SLC6A14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A14 BINDING SITE, designated SEQ ID:14105, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50944] Another function of VGAM1466 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter), Member 14 (SLC6A14, Accession NM_007231). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A14. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_014418) is another VGAM1466 host target gene. TCL6 BINDING SITE1 through TCL6 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 through TCL6 BINDING SITE4, designated SEQ

ID:15771, SEQ ID:21764, SEQ ID:21773 and SEQ ID:14847 respectively, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50945] Another function of VGAM1466 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_014418). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. TUSP (Accession NM_020245) is another VGAM1466 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21537, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50946] Another function of VGAM1466 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. Wingless-type MMTV Integration Site Family, Member 10A

(WNT10A, Accession NM_025216) is another VGAM1466 host target gene. WNT10A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WNT10A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT10A BINDING SITE, designated SEQ ID:24895, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50947] Another function of VGAM1466 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 10A (WNT10A, Accession NM_025216). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT10A. ZF5128 (Accession NM_014347) is another VGAM1466 host target gene. ZF5128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZF5128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZF5128 BINDING SITE, designated SEQ ID:15672, to the nucleotide

sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50948] Another function of VGAM1466 is therefore inhibition of ZF5128 (Accession NM_014347). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZF5128. ZFP106 (Accession NM_022473) is another VGAM1466 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22837, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50949] Another function of VGAM1466 is therefore inhibition of ZFP106 (Accession NM_022473). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC112817 (Accession NM_138413) is another VGAM1466 host target gene. LOC112817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC112817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112817 BINDING SITE, designated SEQ ID:28783, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50950] Another function of VGAM1466 is therefore inhibition of LOC112817 (Accession NM_138413). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112817. LOC121504 (Accession XM_058571) is another VGAM1466 host target gene. LOC121504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC121504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC121504 BINDING SITE, designated SEQ ID:36671, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50951] Another function of VGAM1466 is therefore inhibition of LOC121504 (Accession XM_058571). Accordingly, utilities

of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC121504. LOC128989 (Accession XM_059310) is another VGAM1466 host target gene. LOC128989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36947, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50952] Another function of VGAM1466 is therefore inhibition of LOC128989 (Accession XM_059310). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128989. LOC135818 (Accession XM_059804) is another VGAM1466 host target gene. LOC135818 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC135818 BINDING SITE, designated SEQ ID:37097, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50953] Another function of VGAM1466 is therefore inhibition of LOC135818 (Accession XM_059804). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135818. LOC145371 (Accession XM_085123) is another VGAM1466 host target gene. LOC145371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145371 BINDING SITE, designated SEQ ID:37850, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50954] Another function of VGAM1466 is therefore inhibition of LOC145371 (Accession XM_085123). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145371. LOC145678 (Accession XM_096832) is another VGAM1466 host target gene. LOC145678 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145678 BINDING SITE, designated SEQ ID:40556, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50955] Another function of VGAM1466 is therefore inhibition of LOC145678 (Accession XM_096832). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145678. LOC145813 (Accession XM_096873) is another VGAM1466 host target gene. LOC145813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145813 BINDING SITE, designated SEQ ID:40599, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50956] Another function of VGAM1466 is therefore inhibition of

LOC145813 (Accession XM_096873). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145813. LOC146894 (Accession NM_145273) is another VGAM1466 host target gene. LOC146894 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146894, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146894 BINDING SITE, designated SEQ ID:29785, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50957] Another function of VGAM1466 is therefore inhibition of LOC146894 (Accession NM_145273). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146894. LOC146909 (Accession XM_085634) is another VGAM1466 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38271, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50958] Another function of VGAM1466 is therefore inhibition of LOC146909 (Accession XM_085634). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146909. LOC148887 (Accession XM_097537) is another VGAM1466 host target gene. LOC148887 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148887, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148887 BINDING SITE, designated SEQ ID:40913, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50959] Another function of VGAM1466 is therefore inhibition of LOC148887 (Accession XM_097537). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148887. LOC152018 (Accession XM_098156) is an-

other VGAM1466 host target gene. LOC152018 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152018 BINDING SITE, designated SEQ ID:41424, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50960] Another function of VGAM1466 is therefore inhibition of LOC152018 (Accession XM_098156). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152018. LOC153077 (Accession XM_098307) is another VGAM1466 host target gene. LOC153077 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153077 BINDING SITE, designated SEQ ID:41571, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50961] Another function of VGAM1466 is therefore inhibition of LOC153077 (Accession XM_098307). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153077. LOC153454 (Accession XM_087672) is another VGAM1466 host target gene. LOC153454 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153454 BINDING SITE, designated SEQ ID:39377, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50962] Another function of VGAM1466 is therefore inhibition of LOC153454 (Accession XM_087672). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153454. LOC154877 (Accession XM_098626) is another VGAM1466 host target gene. LOC154877 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC154877, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154877 BINDING SITE, designated SEQ ID:41747, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50963] Another function of VGAM1466 is therefore inhibition of LOC154877 (Accession XM_098626). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154877. LOC158476 (Accession XM_098955) is another VGAM1466 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:42001, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50964] Another function of VGAM1466 is therefore inhibition of LOC158476 (Accession XM_098955). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158476. LOC158865 (Accession XM_099000) is another VGAM1466 host target gene. LOC158865 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158865 BINDING SITE, designated SEQ ID:42039, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50965] Another function of VGAM1466 is therefore inhibition of LOC158865 (Accession XM_099000). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158865. LOC162333 (Accession XM_102591) is another VGAM1466 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42138, to the nucleotide sequence of VGAM1466 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4177.

[50966] Another function of VGAM1466 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC164955 (Accession XM_092265) is another VGAM1466 host target gene. LOC164955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164955 BINDING SITE, designated SEQ ID:40113, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50967] Another function of VGAM1466 is therefore inhibition of LOC164955 (Accession XM_092265). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164955. LOC169225 (Accession XM_108531) is another VGAM1466 host target gene. LOC169225 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169225, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169225 BINDING SITE, designated SEQ ID:42205, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50968] Another function of VGAM1466 is therefore inhibition of LOC169225 (Accession XM_108531). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169225. LOC196529 (Accession XM_113746) is another VGAM1466 host target gene. LOC196529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196529 BINDING SITE, designated SEQ ID:42412, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50969] Another function of VGAM1466 is therefore inhibition of LOC196529 (Accession XM_113746). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196529. LOC199786 (Accession XM_114021) is another VGAM1466 host target gene. LOC199786 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199786 BINDING SITE, designated SEQ ID:42623, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50970] Another function of VGAM1466 is therefore inhibition of LOC199786 (Accession XM_114021). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199786. LOC200316 (Accession XM_114205) is another VGAM1466 host target gene. LOC200316 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200316 BINDING SITE, designated SEQ ID:42796, to the nucleotide sequence of VGAM1466 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4177.

[50971] Another function of VGAM1466 is therefore inhibition of LOC200316 (Accession XM_114205). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200316. LOC200982 (Accession XM_117305) is another VGAM1466 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43379, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50972] Another function of VGAM1466 is therefore inhibition of LOC200982 (Accession XM_117305). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. LOC201626 (Accession XM_114349) is another VGAM1466 host target gene. LOC201626 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201626, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201626 BINDING SITE, designated SEQ ID:42892, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50973] Another function of VGAM1466 is therefore inhibition of LOC201626 (Accession XM_114349). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201626. LOC203197 (Accession XM_114645) is another VGAM1466 host target gene. LOC203197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203197 BINDING SITE, designated SEQ ID:43013, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50974] Another function of VGAM1466 is therefore inhibition of LOC203197 (Accession XM_114645). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC203197. LOC220064 (Accession XM_167827) is another VGAM1466 host target gene. LOC220064 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220064 BINDING SITE, designated SEQ ID:44870, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50975] Another function of VGAM1466 is therefore inhibition of LOC220064 (Accession XM_167827). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220064. LOC220074 (Accession NM_145309) is another VGAM1466 host target gene. LOC220074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220074 BINDING SITE, designated SEQ ID:29825, to

the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50976] Another function of VGAM1466 is therefore inhibition of LOC220074 (Accession NM_145309). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220074. LOC221964 (Accession XM_168342) is another VGAM1466 host target gene. LOC221964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221964 BINDING SITE, designated SEQ ID:45114, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50977] Another function of VGAM1466 is therefore inhibition of LOC221964 (Accession XM_168342). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221964. LOC222031 (Accession XM_168371) is another VGAM1466 host target gene. LOC222031 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC222031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222031 BINDING SITE, designated SEQ ID:45138, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50978] Another function of VGAM1466 is therefore inhibition of LOC222031 (Accession XM_168371). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222031. LOC222224 (Accession XM_168473) is another VGAM1466 host target gene. LOC222224 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222224 BINDING SITE, designated SEQ ID:45198, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50979] Another function of VGAM1466 is therefore inhibition of LOC222224 (Accession XM_168473). Accordingly, utilities

of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222224. LOC253981 (Accession XM_171064) is another VGAM1466 host target gene. LOC253981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253981 BINDING SITE, designated SEQ ID:45868, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50980] Another function of VGAM1466 is therefore inhibition of LOC253981 (Accession XM_171064). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253981. LOC254057 (Accession XM_173085) is another VGAM1466 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC254057 BINDING SITE, designated SEQ ID:46351, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50981] Another function of VGAM1466 is therefore inhibition of LOC254057 (Accession XM_173085). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254057. LOC256306 (Accession XM_172976) is another VGAM1466 host target gene. LOC256306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256306 BINDING SITE, designated SEQ ID:46240, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50982] Another function of VGAM1466 is therefore inhibition of LOC256306 (Accession XM_172976). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256306. LOC257127 (Accession XM_172975) is another VGAM1466 host target gene. LOC257127 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257127 BINDING SITE, designated SEQ ID:46232, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50983] Another function of VGAM1466 is therefore inhibition of LOC257127 (Accession XM_172975). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257127. LOC51008 (Accession NM_015947) is another VGAM1466 host target gene. LOC51008 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51008, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51008 BINDING SITE, designated SEQ ID:18065, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50984] Another function of VGAM1466 is therefore inhibition of

LOC51008 (Accession NM_015947). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51008. LOC90288 (Accession XM_030669) is another VGAM1466 host target gene. LOC90288 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90288, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90288 BINDING SITE, designated SEQ ID:31117, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50985] Another function of VGAM1466 is therefore inhibition of LOC90288 (Accession XM_030669). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90288. LOC90459 (Accession XM_031826) is another VGAM1466 host target gene. LOC90459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC90459 BINDING SITE, designated SEQ ID:31494, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50986] Another function of VGAM1466 is therefore inhibition of LOC90459 (Accession XM_031826). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90459. LOC96597 (Accession XM_039922) is another VGAM1466 host target gene. LOC96597 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC96597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96597 BINDING SITE, designated SEQ ID:33231, to the nucleotide sequence of VGAM1466 RNA, herein designated VGAM RNA, also designated SEQ ID:4177.

[50987] Another function of VGAM1466 is therefore inhibition of LOC96597 (Accession XM_039922). Accordingly, utilities of VGAM1466 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96597. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1467 (VGAM1467) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[50988] VGAM1467 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1467 was detected is described hereinabove with reference to Figs. 1–8.

[50989] VGAM1467 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 2. VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[50990] VGAM1467 gene encodes a VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1467 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1467 precursor RNA is designated SEQ ID:1453, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1453 is located at position 40183 relative to the genome of Equine Herpesvirus 2.

[50991] VGAM1467 precursor RNA folds onto itself, forming VGAM1467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[50992] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1467 folded precursor RNA into VGAM1467 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1467 RNA is designated SEQ ID:4178, and is provided hereinbelow with reference to the sequence listing part.

[50993] VGAM1467 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1467 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[50994] VGAM1467 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1467 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1467 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1467 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[50995] The complementary binding of VGAM1467 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1467 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1467 host target RNA into VGAM1467 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[50996] It is appreciated that VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1467 host target genes. The mRNA of each one of this plurality of VGAM1467 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1467 RNA, herein designated VGAM RNA, and which when bound by VGAM1467 RNA causes inhibition of translation of respective one or more

VGAM1467 host target proteins.

[50997] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1467 gene, herein designated VGAM GENE, on one or more VGAM1467 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[50998] It is yet further appreciated that a function of VGAM1467 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Spe-

cific functions, and accordingly utilities, of VGAM1467 correlate with, and may be deduced from, the identity of the host target genes which VGAM1467 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[50999] Nucleotide sequences of the VGAM1467 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1467 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1467 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1467 are further described hereinbelow with reference to Table 1.

[51000] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1467 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1467 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51001] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1467 gene, herein designated VGAM is inhibition of expression of VGAM1467 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1467 correlate with, and may be deduced from, the identity of the target genes which VGAM1467 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51002] BCL2-like 2 (BCL2L2, Accession NM_004050) is a VGAM1467 host target gene. BCL2L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL2L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L2 BINDING SITE, designated SEQ ID:10259, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51003] A function of VGAM1467 is therefore inhibition of BCL2-like 2 (BCL2L2, Accession NM_004050), a gene which promotes cell survival. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L2. The function of BCL2L2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM431. Cyclin-dependent Kinase 2 (CDK2,

Accession NM_001798) is another VGAM1467 host target gene. CDK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK2 BINDING SITE, designated SEQ ID:7551, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51004] Another function of VGAM1467 is therefore inhibition of Cyclin-dependent Kinase 2 (CDK2, Accession NM_001798), a gene which plays a unique role in cell cycle regulation of vertebrate cells. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK2. The function of CDK2 has been established by previous studies. The complex formed of p34(cdc2) (OMIM Ref. No. 116940) and cyclin B (OMIM Ref. No. 176740) is required for the G2-to-M transition in cell division. Human cyclin A (OMIM Ref. No. 123835) binds independently to 2 kinases, p34(cdc2) or p33. In adenovirus-transformed cells, the viral E1A oncoprotein seems to associate with p33/cyclin A but not with p34(cdc2)/cyclin A. Tsai et al. (1991) isolated

the gene for p33, which shares 65% sequence identity with p34(cdc2). They suggested that p33(cdk2) plays a unique role in cell cycle regulation of vertebrate cells. CDK (e.g., CDK2) activation requires association with cyclins (e.g., CCNE1; 123837) and phosphorylation by CAK (CCNH; 601953), and leads to cell proliferation. Inhibition of cellular proliferation occurs upon association of CDK inhibitor (e.g., CDKN1B; 600778) with a cyclin-CDK complex. Sheaff et al. (1997) showed that expression of CCNE1-CDK2 at physiologic levels of ATP results in phosphorylation of CDKN1B at thr187, leading to elimination of CDKN1B from the cell and progression of the cell cycle from G1 to S phase. At low ATP levels, the inhibitory functions of CDKN1B are enhanced, thereby arresting cell proliferation.

[51005] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51006] Sheaff, R. J.; Groudine, M.; Gordon, M.; Roberts, J. M.; Clurman, B. E. : Cyclin E-CDK2 is a regulator of p27(Kip1). *Genes Dev.* 11: 1464-1478, 1997. ; and

[51007] Tsai, L.-H.; Harlow, E.; Meyerson, M. : Isolation of the human cdk2 gene that encodes the cyclin A- and adenovirus

E1A-associated p33 kinase. Nature 353: 174–177, 1991.

[51008] Further studies establishing the function and utilities of CDK2 are found in John Hopkins OMIM database record ID 116953, and in cited publications numbered 335, 12055–12056, 159, 1496, 4704, 712 and 4705–368 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391) is another VGAM1467 host target gene. CYP8B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP8B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP8B1 BINDING SITE, designated SEQ ID:10628, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51009] Another function of VGAM1467 is therefore inhibition of Cytochrome P450, Subfamily VIII B (sterol 12- α -hydroxylase), Polypeptide 1 (CYP8B1, Accession NM_004391), a gene which functions in bile acid biosynthesis. Accordingly, utilities of VGAM1467 include diag-

nosis, prevention and treatment of diseases and clinical conditions associated with CYP8B1. The function of CYP8B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM923. Giant Axonal Neuropathy (gigaxonin) (GAN, Accession NM_022041) is another VGAM1467 host target gene. GAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAN BINDING SITE, designated SEQ ID:22563, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51010] Another function of VGAM1467 is therefore inhibition of Giant Axonal Neuropathy (gigaxonin) (GAN, Accession NM_022041), a gene which plays an important role in neurofilament architecture. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAN. The function of GAN and its association with various diseases and clinical conditions, has been established by

previous studies, as described hereinabove with reference to VGAM606.Kinesin Family Member C3 (KIFC3, Accession NM_005550) is another VGAM1467 host target gene.

KIFC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIFC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIFC3 BINDING SITE, designated SEQ ID:12080, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51011] Another function of VGAM1467 is therefore inhibition of Kinesin Family Member C3 (KIFC3, Accession NM_005550), a gene which may function in intracellular transport and mitosis. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIFC3. The function of KIFC3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1006.Nyctalopin (NYX, Accession NM_022567) is another VGAM1467 host target gene. NYX BINDING SITE1 and NYX BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by NYX, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYX BINDING SITE1 and NYX BINDING SITE2, designated SEQ ID:22887 and SEQ ID:22888 respectively, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51012] Another function of VGAM1467 is therefore inhibition of Nyctalopin (NYX, Accession NM_022567), a gene which functions as the von willebrand factor receptor and mediates von willebrand factor-dependent platelet adhesion to blood vessels. the adhesion of platelets to injured vascular surfaces in the arterial circulation is a critical initiating event in hemostasis (by similarity). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYX. The function of NYX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206. Promyelocytic Leukemia (PML, Accession NM_033240) is another VGAM1467 host target gene. PML BINDING SITE1 and PML BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by PML, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE1 and PML BINDING SITE2, designated SEQ ID:27082 and SEQ ID:27086 respectively, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51013] Another function of VGAM1467 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM_033240). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. Paired Mesoderm Homeo Box 1 (PMX1, Accession NM_006902) is another VGAM1467 host target gene. PMX1 BINDING SITE1 and PMX1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PMX1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMX1 BINDING SITE1 and PMX1 BINDING SITE2, designated SEQ ID:13778 and SEQ ID:12907 respectively, to the nu-

cleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51014] Another function of VGAM1467 is therefore inhibition of Paired Mesoderm Homeo Box 1 (PMX1, Accession NM_006902), a gene which acts as a transcriptional regulator of muscle creatine kinase. Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMX1. The function of PMX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM381.FLJ13189 (Accession NM_024882) is another VGAM1467 host target gene. FLJ13189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13189 BINDING SITE, designated SEQ ID:24330, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51015] Another function of VGAM1467 is therefore inhibition of FLJ13189 (Accession NM_024882). Accordingly, utilities of

VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13189. Glycoprotein V (platelet) (GP5, Accession NM_004488) is another VGAM1467 host target gene. GP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GP5 BINDING SITE, designated SEQ ID:10815, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51016] Another function of VGAM1467 is therefore inhibition of Glycoprotein V (platelet) (GP5, Accession NM_004488). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GP5. Interleukin 1 Family, Member 10 (theta) (IL1F10, Accession NM_032556) is another VGAM1467 host target gene. IL1F10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL1F10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of IL1F10 BINDING SITE, designated SEQ ID:26283, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51017] Another function of VGAM1467 is therefore inhibition of Interleukin 1 Family, Member 10 (theta) (IL1F10, Accession NM_032556). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F10. KIAA0935 (Accession XM_052620) is another VGAM1467 host target gene. KIAA0935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0935 BINDING SITE, designated SEQ ID:36009, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51018] Another function of VGAM1467 is therefore inhibition of KIAA0935 (Accession XM_052620). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0935. KIAA1388 (Accession XM_168030) is another VGAM1467 host target gene. KIAA1388 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1388 BINDING SITE, designated SEQ ID:44951, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51019] Another function of VGAM1467 is therefore inhibition of KIAA1388 (Accession XM_168030). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1388. KIAA1674 (Accession XM_044065) is another VGAM1467 host target gene. KIAA1674 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1674 BINDING SITE, designated SEQ ID:34103, to the nucleotide sequence of VGAM1467 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4178.

[51020] Another function of VGAM1467 is therefore inhibition of KIAA1674 (Accession XM_044065). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1674. Neuroblastoma, Suppression of Tumorigenicity 1 (NBL1, Accession XM_001434) is another VGAM1467 host target gene. NBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NBL1 BINDING SITE, designated SEQ ID:29837, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51021] Another function of VGAM1467 is therefore inhibition of Neuroblastoma, Suppression of Tumorigenicity 1 (NBL1, Accession XM_001434). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NBL1. Nei Like 2 (E. coli) (NEIL2, Accession NM_145043) is another VGAM1467 host target gene. NEIL2 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NEIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEIL2 BINDING SITE, designated SEQ ID:29672, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51022] Another function of VGAM1467 is therefore inhibition of Nei Like 2 (E. coli) (NEIL2, Accession NM_145043). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEIL2. PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975) is another VGAM1467 host target gene. PTK6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK6 BINDING SITE, designated SEQ ID:12600, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51023] Another function of VGAM1467 is therefore inhibition of PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK6. RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM_013401) is another VGAM1467 host target gene. RAB3IL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3IL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3IL1 BINDING SITE, designated SEQ ID:15061, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51024] Another function of VGAM1467 is therefore inhibition of RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM_013401). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3IL1. SEC24 Related Gene Family, Member A (*S. cerevisiae*) (SEC24A, Accession XM_094581) is another VGAM1467 host target gene. SEC24A BINDING SITE is HOST TARGET binding site found

in the 5' untranslated region of mRNA encoded by SEC24A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC24A BINDING SITE, designated SEQ ID:40234, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51025] Another function of VGAM1467 is therefore inhibition of SEC24 Related Gene Family, Member A (*S. cerevisiae*) (SEC24A, Accession XM_094581). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC24A. Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM_006671) is another VGAM1467 host target gene. SLC1A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A7 BINDING SITE, designated SEQ ID:13488, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM

RNA, also designated SEQ ID:4178.

[51026] Another function of VGAM1467 is therefore inhibition of Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM_006671). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A7. STRAIT11499 (Accession NM_021242) is another VGAM1467 host target gene. STRAIT11499 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STRAIT11499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRAIT11499 BINDING SITE, designated SEQ ID:22208, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51027] Another function of VGAM1467 is therefore inhibition of STRAIT11499 (Accession NM_021242). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRAIT11499. LOC145988 (Accession XM_085290) is another VGAM1467 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38035, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51028] Another function of VGAM1467 is therefore inhibition of LOC145988 (Accession XM_085290). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC148529 (Accession XM_097481) is another VGAM1467 host target gene. LOC148529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148529 BINDING SITE, designated SEQ ID:40889, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51029] Another function of VGAM1467 is therefore inhibition of LOC148529 (Accession XM_097481). Accordingly, utilities

of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148529. LOC150407 (Accession XM_086906) is another VGAM1467 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38951, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51030] Another function of VGAM1467 is therefore inhibition of LOC150407 (Accession XM_086906). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC157567 (Accession XM_088328) is another VGAM1467 host target gene. LOC157567 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC157567 BINDING SITE, designated SEQ ID:39613, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51031] Another function of VGAM1467 is therefore inhibition of LOC157567 (Accession XM_088328). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157567. LOC159121 (Accession XM_099028) is another VGAM1467 host target gene. LOC159121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159121 BINDING SITE, designated SEQ ID:42064, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51032] Another function of VGAM1467 is therefore inhibition of LOC159121 (Accession XM_099028). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159121. LOC196812 (Accession XM_116868) is another VGAM1467 host target gene. LOC196812 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43137, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51033] Another function of VGAM1467 is therefore inhibition of LOC196812 (Accession XM_116868). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC199923 (Accession XM_114057) is another VGAM1467 host target gene. LOC199923 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199923 BINDING SITE, designated SEQ ID:42666, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51034] Another function of VGAM1467 is therefore inhibition of

LOC199923 (Accession XM_114057). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199923. LOC92465 (Accession XM_045250) is another VGAM1467 host target gene. LOC92465 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92465 BINDING SITE, designated SEQ ID:34391, to the nucleotide sequence of VGAM1467 RNA, herein designated VGAM RNA, also designated SEQ ID:4178.

[51035] Another function of VGAM1467 is therefore inhibition of LOC92465 (Accession XM_045250). Accordingly, utilities of VGAM1467 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92465. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1468 (VGAM1468) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[51036] VGAM1468 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1468 was detected is described hereinabove with reference to Figs. 1–8.

[51037] VGAM1468 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Flacherie Virus. VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51038] VGAM1468 gene encodes a VGAM1468 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1468 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1468 precursor RNA is designated SEQ ID:1454, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1454 is located at position 4200 relative to the genome of Infectious Flacherie Virus.

[51039] VGAM1468 precursor RNA folds onto itself, forming VGAM1468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two–

dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51040] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1468 folded precursor RNA into VGAM1468 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1468 RNA is designated SEQ ID:4179, and is provided hereinbelow with reference to the sequence listing part.

[51041] VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1468 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein cod-

ing region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[51042] VGAM1468 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1468 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1468 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[51043] The complementary binding of VGAM1468 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1468 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1468 host target RNA into VGAM1468 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51044] It is appreciated that VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1468 host target genes. The mRNA of each one of this plurality of VGAM1468 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1468 RNA, herein designated VGAM RNA, and which when bound by VGAM1468 RNA causes inhibition of translation of respective one or more VGAM1468 host target proteins.

[51045] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1468 gene, herein designated VGAM GENE, on one

or more VGAM1468 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51046] It is yet further appreciated that a function of VGAM1468 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of viral infection by Infectious Flacherie Virus. Specific functions, and accordingly utilities, of VGAM1468 correlate with, and may be deduced from, the identity of the host target genes which VGAM1468 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51047] Nucleotide sequences of the VGAM1468 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1468 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1468 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1468 are further described hereinbelow with reference to Table 1.

[51048] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1468 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1468 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51049] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1468 gene, herein designated VGAM is inhibition of expression of VGAM1468 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1468 correlate with, and may be deduced from, the identity of the target genes which VGAM1468 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51050] Ankyrin Repeat Domain 6 (ANKRD6, Accession

NM_014942) is a VGAM1468 host target gene. ANKRD6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANKRD6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANKRD6 BINDING SITE, designated SEQ ID:17251, to the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, also designated SEQ ID:4179.

[51051] A function of VGAM1468 is therefore inhibition of Ankyrin Repeat Domain 6 (ANKRD6, Accession NM_014942). Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANKRD6. FLJ10853 (Accession NM_018246) is another VGAM1468 host target gene. FLJ10853 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated SEQ ID:20212, to the nucleotide sequence of VGAM1468 RNA,

herein designated VGAM RNA, also designated SEQ ID:4179.

[51052] Another function of VGAM1468 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. FLJ22625 (Accession NM_024715) is another VGAM1468 host target gene. FLJ22625 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22625, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22625 BINDING SITE, designated SEQ ID:24040, to the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, also designated SEQ ID:4179.

[51053] Another function of VGAM1468 is therefore inhibition of FLJ22625 (Accession NM_024715). Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22625. KIAA0446 (Accession XM_044155) is another VGAM1468 host target gene. KIAA0446 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34152, to the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, also designated SEQ ID:4179.

[51054] Another function of VGAM1468 is therefore inhibition of KIAA0446 (Accession XM_044155). Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0446. LOC126964 (Accession XM_059100) is another VGAM1468 host target gene. LOC126964 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126964, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126964 BINDING SITE, designated SEQ ID:36881, to the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, also designated SEQ ID:4179.

[51055] Another function of VGAM1468 is therefore inhibition of LOC126964 (Accession XM_059100). Accordingly, utilities

of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126964. LOC158476 (Accession XM_098955) is another VGAM1468 host target gene. LOC158476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158476 BINDING SITE, designated SEQ ID:41994, to the nucleotide sequence of VGAM1468 RNA, herein designated VGAM RNA, also designated SEQ ID:4179.

[51056] Another function of VGAM1468 is therefore inhibition of LOC158476 (Accession XM_098955). Accordingly, utilities of VGAM1468 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158476. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1469 (VGAM1469) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51057] VGAM1469 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1469 was detected is described hereinabove with reference to Figs. 1-8.

[51058] VGAM1469 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Infectious Flacherie Virus. VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51059] VGAM1469 gene encodes a VGAM1469 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1469 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1469 precursor RNA is designated SEQ ID:1455, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1455 is located at position 916 relative to the genome of Infectious Flacherie Virus.

[51060] VGAM1469 precursor RNA folds onto itself, forming VGAM1469 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51061] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1469 folded precursor RNA into VGAM1469 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM1469 RNA is designated SEQ ID:4180, and is provided hereinbelow with reference to the sequence listing part.

[51062] VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1469 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[51063] VGAM1469 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1469 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1469 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51064] The complementary binding of VGAM1469 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1469 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1469 host target RNA into VGAM1469 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51065] It is appreciated that VGAM1469 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1469 host target genes. The mRNA of each one of this plurality of VGAM1469 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1469 RNA, herein designated VGAM RNA, and which when bound by VGAM1469 RNA causes inhibition of translation of respective one or more VGAM1469 host target proteins.

[51066] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1469 gene, herein designated VGAM GENE, on one or more VGAM1469 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51067] It is yet further appreciated that a function of VGAM1469 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of viral infection by Infectious Flacherie Virus. Specific functions, and accordingly utilities, of VGAM1469 correlate with, and may be deduced from, the identity of the host target genes which VGAM1469 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51068] Nucleotide sequences of the VGAM1469 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1469 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1469 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1469 are further
described hereinbelow with reference to Table 1.

[51069] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1469 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1469 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[51070] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1469 gene, herein designated VGAM is
inhibition of expression of VGAM1469 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1469 correlate with, and may be deduced
from, the identity of the target genes which VGAM1469
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[51071] Vacuolar Protein Sorting 41 (yeast) (VPS41, Accession
NM_014396) is a VGAM1469 host target gene. VPS41

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS41 BINDING SITE, designated SEQ ID:15735, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51072] A function of VGAM1469 is therefore inhibition of Vacuolar Protein Sorting 41 (yeast) (VPS41, Accession NM_014396). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS41. DKFZp547I224 (Accession NM_020221) is another VGAM1469 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21472, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51073] Another function of VGAM1469 is therefore inhibition of DKFZp547I224 (Accession NM_020221). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I224. KIAA0916 (Accession NM_015057) is another VGAM1469 host target gene. KIAA0916 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0916 BINDING SITE, designated SEQ ID:17415, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51074] Another function of VGAM1469 is therefore inhibition of KIAA0916 (Accession NM_015057). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0916. PAI-RBP1 (Accession NM_015640) is another VGAM1469 host target gene. PAI-RBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PAI-RBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAI-RBP1 BINDING SITE, designated SEQ ID:17892, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51075] Another function of VGAM1469 is therefore inhibition of PAI-RBP1 (Accession NM_015640). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAI-RBP1. PRO1992 (Accession NM_014107) is another VGAM1469 host target gene. PRO1992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1992 BINDING SITE, designated SEQ ID:15332, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51076] Another function of VGAM1469 is therefore inhibition of PRO1992 (Accession NM_014107). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PRO1992. LOC112476 (Accession NM_145239) is another VGAM1469 host target gene. LOC112476 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112476 BINDING SITE, designated SEQ ID:29750, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51077] Another function of VGAM1469 is therefore inhibition of LOC112476 (Accession NM_145239). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112476. LOC147219 (Accession XM_097214) is another VGAM1469 host target gene. LOC147219 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147219, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147219 BINDING SITE, designated SEQ ID:40822, to the nucleotide sequence of VGAM1469 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4180.

[51078] Another function of VGAM1469 is therefore inhibition of LOC147219 (Accession XM_097214). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147219. LOC150139 (Accession XM_086794) is another VGAM1469 host target gene. LOC150139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150139 BINDING SITE, designated SEQ ID:38856, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51079] Another function of VGAM1469 is therefore inhibition of LOC150139 (Accession XM_086794). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150139. LOC150157 (Accession XM_097823) is another VGAM1469 host target gene. LOC150157 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150157, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150157 BINDING SITE, designated SEQ ID:41139, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51080] Another function of VGAM1469 is therefore inhibition of LOC150157 (Accession XM_097823). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150157. LOC152502 (Accession XM_001389) is another VGAM1469 host target gene. LOC152502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152502 BINDING SITE, designated SEQ ID:29834, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51081] Another function of VGAM1469 is therefore inhibition of LOC152502 (Accession XM_001389). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152502. LOC196890 (Accession XM_116951) is another VGAM1469 host target gene. LOC196890 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196890, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196890 BINDING SITE, designated SEQ ID:43154, to the nucleotide sequence of VGAM1469 RNA, herein designated VGAM RNA, also designated SEQ ID:4180.

[51082] Another function of VGAM1469 is therefore inhibition of LOC196890 (Accession XM_116951). Accordingly, utilities of VGAM1469 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196890. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1470 (VGAM1470) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51083] VGAM1470 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1470 was detected is described hereinabove with reference to Figs. 1–8.

[51084] VGAM1470 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51085] VGAM1470 gene encodes a VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1470 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1470 precursor RNA is designated SEQ ID:1456, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1456 is located at position 5947 relative to the genome of Cocksfoot Streak Virus (CSV).

[51086] VGAM1470 precursor RNA folds onto itself, forming VGAM1470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51087] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1470 folded precursor RNA into VGAM1470 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1470 RNA is designated SEQ ID:4181, and is provided hereinbelow with reference to the sequence listing part.

[51088] VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1470 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51089] VGAM1470 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1470 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1470 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51090] The complementary binding of VGAM1470 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1470 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1470 host target RNA into VGAM1470 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51091] It is appreciated that VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1470 host target genes. The mRNA of each one of this plurality of VGAM1470 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1470 RNA, herein designated VGAM RNA, and which when bound by VGAM1470 RNA causes inhibition of translation of respective one or more VGAM1470 host target proteins.

[51092] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1470 gene, herein designated VGAM GENE, on one or more VGAM1470 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51093] It is yet further appreciated that a function of VGAM1470 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1470 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1470 correlate with, and may be deduced from, the identity of the host target genes which VGAM1470 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51094] Nucleotide sequences of the VGAM1470 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1470 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1470 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1470 are further described hereinbelow with reference to Table 1.

[51095] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1470 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1470 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51096] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1470 gene, herein designated VGAM is inhibition of expression of VGAM1470 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1470 correlate with, and may be deduced from, the identity of the target genes which VGAM1470 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51097] Fms-related Tyrosine Kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1, Accession NM_002019) is a VGAM1470 host target gene.

FLT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLT1 BINDING SITE, designated SEQ ID:7764, to the nucleotide sequence of VGAM1470 RNA, herein designated VGAM RNA, also designated SEQ ID:4181.

[51098] A function of VGAM1470 is therefore inhibition of Fms-related Tyrosine Kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1, Accession NM_002019). Accordingly, utilities of VGAM1470 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLT1. Transcriptional Intermediary Factor 1 (TIF1, Accession XM_016701) is another VGAM1470 host target gene. TIF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIF1 BINDING SITE, designated SEQ ID:30275, to the nucleotide sequence of VGAM1470 RNA, herein designated VGAM RNA,

also designated SEQ ID:4181.

[51099] Another function of VGAM1470 is therefore inhibition of Transcriptional Intermediary Factor 1 (TIF1, Accession XM_016701), a gene which mediates the activation function (AF-2) of nuclear estrogen receptor. Accordingly, utilities of VGAM1470 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIF1. The function of TIF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM108.FLJ14600 (Accession NM_032810) is another VGAM1470 host target gene. FLJ14600 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14600 BINDING SITE, designated SEQ ID:26575, to the nucleotide sequence of VGAM1470 RNA, herein designated VGAM RNA, also designated SEQ ID:4181.

[51100] Another function of VGAM1470 is therefore inhibition of FLJ14600 (Accession NM_032810). Accordingly, utilities of VGAM1470 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with FLJ14600. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1471 (VGAM1471) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51101] VGAM1471 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1471 was detected is described hereinabove with reference to Figs. 1–8.

[51102] VGAM1471 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51103] VGAM1471 gene encodes a VGAM1471 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1471 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1471 precursor RNA is desig-

nated SEQ ID:1457, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1457 is located at position 4782 relative to the genome of Cocksfoot Streak Virus (CSV).

- [51104] VGAM1471 precursor RNA folds onto itself, forming VGAM1471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51105] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1471 folded precursor RNA into VGAM1471 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM1471 RNA is designated SEQ ID:4182, and is provided hereinbelow with reference to the sequence

listing part.

[51106] VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1471 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51107] VGAM1471 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1471 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1471 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51108] The complementary binding of VGAM1471 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1471 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1471 host target RNA into VGAM1471 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51109] It is appreciated that VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1471 host target genes. The mRNA of each one of this plurality of VGAM1471 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1471 RNA, herein designated VGAM

RNA, and which when bound by VGAM1471 RNA causes inhibition of translation of respective one or more VGAM1471 host target proteins.

[51110] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1471 gene, herein designated VGAM GENE, on one or more VGAM1471 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51111] It is yet further appreciated that a function of VGAM1471 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1471 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1471 correlate with, and may be deduced from, the identity of the host target genes which VGAM1471 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51112] Nucleotide sequences of the VGAM1471 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1471 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1471 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1471 are further described hereinbelow with reference to Table 1.

[51113] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1471 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1471 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51114] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1471 gene, herein designated VGAM is

inhibition of expression of VGAM1471 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1471 correlate with, and may be deduced from, the identity of the target genes which VGAM1471 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51115] Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 1 (NFATC1, Accession NM_006162) is a VGAM1471 host target gene. NFATC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFATC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFATC1 BINDING SITE, designated SEQ ID:12814, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51116] A function of VGAM1471 is therefore inhibition of Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 1 (NFATC1, Accession NM_006162), a gene which regulates the activation, proliferation, differentiation and programmed death of lymphoid and nonlymphoid cells. Accordingly, utilities of VGAM1471 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with NFATC1. The function of NFATC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM123.BTB (POZ) Domain Containing 3 (BTBD3, Accession NM_014962) is another VGAM1471 host target gene. BTBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17337, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51117] Another function of VGAM1471 is therefore inhibition of BTB (POZ) Domain Containing 3 (BTBD3, Accession NM_014962). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. DKFZp761N0624 (Accession NM_032295) is another VGAM1471 host target gene. DKFZp761N0624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by DKFZp761N0624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N0624 BINDING SITE, designated SEQ ID:26074, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51118] Another function of VGAM1471 is therefore inhibition of DKFZp761N0624 (Accession NM_032295). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761N0624. FLJ21709 (Accession XM_085480) is another VGAM1471 host target gene. FLJ21709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21709 BINDING SITE, designated SEQ ID:38169, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51119] Another function of VGAM1471 is therefore inhibition of FLJ21709 (Accession XM_085480). Accordingly, utilities of

VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21709. GTP Binding Protein 5 (putative) (GTPBP5, Accession XM_037206) is another VGAM1471 host target gene. GTPBP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTPBP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTPBP5 BINDING SITE, designated SEQ ID:32574, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51120] Another function of VGAM1471 is therefore inhibition of GTP Binding Protein 5 (putative) (GTPBP5, Accession XM_037206). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTPBP5. MGC21675 (Accession NM_052861) is another VGAM1471 host target gene. MGC21675 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC21675, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21675 BINDING SITE, designated SEQ ID:27444, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51121] Another function of VGAM1471 is therefore inhibition of MGC21675 (Accession NM_052861). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21675. U5-100K (Accession XM_006784) is another VGAM1471 host target gene. U5-100K BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by U5-100K, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of U5-100K BINDING SITE, designated SEQ ID:30011, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51122] Another function of VGAM1471 is therefore inhibition of U5-100K (Accession XM_006784). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

U5-100K. LOC150407 (Accession XM_086906) is another VGAM1471 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38954, to the nucleotide sequence of VGAM1471 RNA, herein designated VGAM RNA, also designated SEQ ID:4182.

[51123] Another function of VGAM1471 is therefore inhibition of LOC150407 (Accession XM_086906). Accordingly, utilities of VGAM1471 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1472 (VGAM1472) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51124] VGAM1472 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1472 was detected is described hereinabove with reference to Figs. 1–8.

[51125] VGAM1472 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51126] VGAM1472 gene encodes a VGAM1472 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1472 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1472 precursor RNA is designated SEQ ID:1458, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1458 is located at position 4423 relative to the genome of Cocksfoot Streak Virus (CSV).

[51127] VGAM1472 precursor RNA folds onto itself, forming VGAM1472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide

sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51128] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1472 folded precursor RNA into VGAM1472 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1472 RNA is designated SEQ ID:4183, and is provided hereinbelow with reference to the sequence listing part.

[51129] VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1472 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51130] VGAM1472 RNA, herein designated VGAM RNA, binds

complementarily to one or more host target binding sites located in untranslated regions of VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1472 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1472 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[51131] The complementary binding of VGAM1472 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM1472 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1472 host target RNA into VGAM1472 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51132] It is appreciated that VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1472 host target genes. The mRNA of each one of this plurality of VGAM1472 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1472 RNA, herein designated VGAM RNA, and which when bound by VGAM1472 RNA causes inhibition of translation of respective one or more VGAM1472 host target proteins.

[51133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1472 gene, herein designated VGAM GENE, on one or more VGAM1472 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51134] It is yet further appreciated that a function of VGAM1472 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1472 correlate with, and may be deduced from, the identity of the host target genes which VGAM1472 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51135] Nucleotide sequences of the VGAM1472 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1472 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM1472 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1472 are further described hereinbelow with reference to Table 1.

[51136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1472 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1472 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51137] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1472 gene, herein designated VGAM is inhibition of expression of VGAM1472 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1472 correlate with, and may be deduced from, the identity of the target genes which VGAM1472 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51138] Protein Kinase, CAMP-dependent, Catalytic, Beta (PRKACB, Accession NM_002731) is a VGAM1472 host target gene. PRKACB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PRKACB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKACB BINDING SITE, designated SEQ ID:8602, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51139] A function of VGAM1472 is therefore inhibition of Protein Kinase, CAMP-dependent, Catalytic, Beta (PRKACB, Accession NM_002731), a gene which is the catalytic beta subunit of cAMP-dependent protein kinase (PKA). Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKACB. The function of PRKACB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM795. Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM1472 host target gene. SEDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of SEDL BINDING SITE, designated SEQ ID:15909, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51140] Another function of VGAM1472 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.Solute Carrier Family 35 (CMP-sialic acid transporter), Member 1 (SLC35A1, Accession NM_006416) is another VGAM1472 host target gene. SLC35A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC35A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC35A1 BINDING SITE, designated SEQ ID:13127, to the nucleotide sequence of VGAM1472 RNA,

herein designated VGAM RNA, also designated SEQ ID:4183.

[51141] Another function of VGAM1472 is therefore inhibition of Solute Carrier Family 35 (CMP-sialic acid transporter), Member 1 (SLC35A1, Accession NM_006416), a gene which transports cmp-sialic acid from the cytosol into golgi vesicles. Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC35A1. The function of SLC35A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Steroid-5-alpha-reductase, Alpha Polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1) (SRD5A1, Accession NM_001047) is another VGAM1472 host target gene. SRD5A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRD5A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRD5A1 BINDING SITE, designated SEQ ID:6716, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4183.

[51142] Another function of VGAM1472 is therefore inhibition of Steroid-5-alpha-reductase, Alpha Polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1) (SRD5A1, Accession NM_001047), a gene which catalyzes the conversion of testosterone into 5-alpha-dihydrotestosterone and progesterone . Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRD5A1. The function of SRD5A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM749.ADMP (Accession NM_145035) is another VGAM1472 host target gene. ADMP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADMP BINDING SITE, designated SEQ ID:29657, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51143] Another function of VGAM1472 is therefore inhibition of

ADMP (Accession NM_145035). Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADMP. KIAA0872 (Accession NM_014940) is another VGAM1472 host target gene. KIAA0872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0872 BINDING SITE, designated SEQ ID:17246, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51144] Another function of VGAM1472 is therefore inhibition of KIAA0872 (Accession NM_014940). Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0872. LOC148137 (Accession NM_144692) is another VGAM1472 host target gene. LOC148137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC148137 BINDING SITE, designated SEQ ID:29516, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51145] Another function of VGAM1472 is therefore inhibition of LOC148137 (Accession NM_144692). Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148137. LOC162333 (Accession XM_102591) is another VGAM1472 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42127, to the nucleotide sequence of VGAM1472 RNA, herein designated VGAM RNA, also designated SEQ ID:4183.

[51146] Another function of VGAM1472 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM1472 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1473 (VGAM1473) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51147] VGAM1473 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1473 was detected is described hereinabove with reference to Figs. 1–8.

[51148] VGAM1473 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51149] VGAM1473 gene encodes a VGAM1473 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1473 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1473 precursor RNA is designated SEQ ID:1459, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1459 is located at position 8361 relative to the genome of Cocksfoot Streak Virus (CSV).

[51150] VGAM1473 precursor RNA folds onto itself, forming VGAM1473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51151] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1473 folded precursor RNA into VGAM1473 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1473 RNA is designated SEQ ID:4184, and is provided hereinbelow with reference to the sequence listing part.

[51152] VGAM1473 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1473 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[51153] VGAM1473 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1473 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1473 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1473 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[51154] The complementary binding of VGAM1473 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1473 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1473 host target RNA into VGAM1473 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51155] It is appreciated that VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1473 host target genes. The mRNA of each one of this plurality of VGAM1473 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1473 RNA, herein designated VGAM RNA, and which when bound by VGAM1473 RNA causes inhibition of translation of respective one or more

VGAM1473 host target proteins.

[51156] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1473 gene, herein designated VGAM GENE, on one or more VGAM1473 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51157] It is yet further appreciated that a function of VGAM1473 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus

(CSV). Specific functions, and accordingly utilities, of VGAM1473 correlate with, and may be deduced from, the identity of the host target genes which VGAM1473 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51158] Nucleotide sequences of the VGAM1473 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1473 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1473 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1473 are further described hereinbelow with reference to Table 1.

[51159] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1473 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1473 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51160] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1473 gene, herein designated VGAM is inhibition of expression of VGAM1473 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1473 correlate with, and may be deduced from, the identity of the target genes which VGAM1473 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51161] FLJ20345 (Accession NM_017777) is a VGAM1473 host target gene. FLJ20345 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20345, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20345 BINDING SITE, designated SEQ ID:19407, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51162] A function of VGAM1473 is therefore inhibition of FLJ20345 (Accession NM_017777). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20345. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM1473 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23711, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51163] Another function of VGAM1473 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. KIAA1061 (Accession XM_048786) is another VGAM1473 host target gene. KIAA1061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1061 BINDING SITE, designated SEQ ID:35268, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51164] Another function of VGAM1473 is therefore inhibition of KIAA1061 (Accession XM_048786). Accordingly, utilities

of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1061. KIAA1300 (Accession XM_031744) is another VGAM1473 host target gene. KIAA1300 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1300 BINDING SITE, designated SEQ ID:31482, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51165] Another function of VGAM1473 is therefore inhibition of KIAA1300 (Accession XM_031744). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1300. PRO1386 (Accession NM_031269) is another VGAM1473 host target gene. PRO1386 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1386

BINDING SITE, designated SEQ ID:25291, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51166] Another function of VGAM1473 is therefore inhibition of PRO1386 (Accession NM_031269). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1386. Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM_014820) is another VGAM1473 host target gene. TOMM70A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOMM70A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOMM70A BINDING SITE, designated SEQ ID:16790, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51167] Another function of VGAM1473 is therefore inhibition of Translocase of Outer Mitochondrial Membrane 70 Homolog A (yeast) (TOMM70A, Accession NM_014820). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with TOMM70A. LOC157931 (Accession XM_098845) is another VGAM1473 host target gene. LOC157931 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157931 BINDING SITE, designated SEQ ID:41903, to the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51168] Another function of VGAM1473 is therefore inhibition of LOC157931 (Accession XM_098845). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157931. LOC222166 (Accession XM_168425) is another VGAM1473 host target gene. LOC222166 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC222166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222166 BINDING SITE, designated SEQ ID:45154, to

the nucleotide sequence of VGAM1473 RNA, herein designated VGAM RNA, also designated SEQ ID:4184.

[51169] Another function of VGAM1473 is therefore inhibition of LOC222166 (Accession XM_168425). Accordingly, utilities of VGAM1473 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222166. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1474 (VGAM1474) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51170] VGAM1474 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1474 was detected is described hereinabove with reference to Figs. 1–8.

[51171] VGAM1474 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51172] VGAM1474 gene encodes a VGAM1474 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1474 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1474 precursor RNA is designated SEQ ID:1460, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1460 is located at position 761 relative to the genome of Cocksfoot Streak Virus (CSV).

- [51173] VGAM1474 precursor RNA folds onto itself, forming VGAM1474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51174] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1474 folded precursor RNA into VGAM1474 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1474 RNA is designated SEQ ID:4185, and is provided hereinbelow with reference to the sequence listing part.

[51175] VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1474 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51176] VGAM1474 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1474 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1474 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51177] The complementary binding of VGAM1474 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1474 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1474 host target RNA into VGAM1474 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51178] It is appreciated that VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM1474 host target genes. The mRNA of each one of this plurality of VGAM1474 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1474 RNA, herein designated VGAM RNA, and which when bound by VGAM1474 RNA causes inhibition of translation of respective one or more VGAM1474 host target proteins.

[51179] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1474 gene, herein designated VGAM GENE, on one or more VGAM1474 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[51180] It is yet further appreciated that a function of VGAM1474 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1474 correlate with, and may be deduced from, the identity of the host target genes which VGAM1474 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51181] Nucleotide sequences of the VGAM1474 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1474 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1474 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1474 are further described hereinbelow with reference to Table 1.

[51182] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1474 host target RNA, and schematic representation of the complementarity of each

of these host target binding sites to VGAM1474 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51183] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1474 gene, herein designated VGAM is inhibition of expression of VGAM1474 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1474 correlate with, and may be deduced from, the identity of the target genes which VGAM1474 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51184] Chondroitin Sulfate Proteoglycan 3 (neurocan) (CSPG3, Accession NM_004386) is a VGAM1474 host target gene. CSPG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSPG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSPG3 BINDING SITE, designated SEQ ID:10615, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51185] A function of VGAM1474 is therefore inhibition of Chon-

droitin Sulfate Proteoglycan 3 (neurocan) (CSPG3, Accession NM_004386), a gene which may play a role in modulating cell adhesion and migration. Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSPG3. The function of CSPG3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM634. Protocadherin Alpha 1 (PCDHA1, Accession NM_018900) is another VGAM1474 host target gene. PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA1 BINDING SITE1 and PCDHA1 BINDING SITE2, designated SEQ ID:20867 and SEQ ID:25386 respectively, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51186] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 1 (PCDHA1, Accession NM_018900). Accordingly, utilities of VGAM1474 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with PCDHA1. Protocadherin Alpha 10 (PCDHA10, Accession NM_018901) is another VGAM1474 host target gene. PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA10 BINDING SITE1 and PCDHA10 BINDING SITE2, designated SEQ ID:20877 and SEQ ID:20888 respectively, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51187] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 10 (PCDHA10, Accession NM_018901). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA10. Protocadherin Alpha 13 (PCDHA13, Accession NM_018904) is another VGAM1474 host target gene. PCDHA13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA13 BINDING SITE, designated SEQ ID:20908, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51188] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 13 (PCDHA13, Accession NM_018904). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA13. Protocadherin Alpha 2 (PCDHA2, Accession NM_018905) is another VGAM1474 host target gene. PCDHA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA2 BINDING SITE, designated SEQ ID:20918, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51189] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 2 (PCDHA2, Accession NM_018905). Accordingly, utilities of VGAM1474 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with PCDHA2. Protocadherin Alpha 3 (PCDHA3, Accession NM_018906) is another VGAM1474 host target gene. PCDHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA3 BINDING SITE, designated SEQ ID:20928, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51190] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 3 (PCDHA3, Accession NM_018906). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA3. Protocadherin Alpha 4 (PCDHA4, Accession NM_018907) is another VGAM1474 host target gene. PCDHA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PCDHA4 BINDING SITE, designated SEQ ID:20938, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51191] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 4 (PCDHA4, Accession NM_018907). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA4. Protocadherin Alpha 5 (PCDHA5, Accession NM_018908) is another VGAM1474 host target gene. PCDHA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA5 BINDING SITE, designated SEQ ID:20948, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51192] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 5 (PCDHA5, Accession NM_018908). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with PCDHA5. Protocadherin Alpha 6 (PCDHA6, Accession NM_018909) is another VGAM1474 host target gene. PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA6 BINDING SITE1 and PCDHA6 BINDING SITE2, designated SEQ ID:20958 and SEQ ID:25590 respectively, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51193] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 6 (PCDHA6, Accession NM_018909). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA6. Protocadherin Alpha 8 (PCDHA8, Accession NM_018911) is another VGAM1474 host target gene. PCDHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PCDHA8 BINDING SITE, designated SEQ ID:20978, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51194] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 8 (PCDHA8, Accession NM_018911). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA8. Protocadherin Alpha 9 (PCDHA9, Accession NM_031857) is another VGAM1474 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:25604, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51195] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_031857), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM1474 include diagno-

sis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM71. Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898) is another VGAM1474 host target gene. PCDHAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC1 BINDING SITE, designated SEQ ID:20847, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51196] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha Subfamily C, 1 (PCDHAC1, Accession NM_018898). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC1. Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899) is another VGAM1474 host target gene. PCDHAC2 BIND-

ING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHAC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHAC2 BINDING SITE, designated SEQ ID:20857, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51197] Another function of VGAM1474 is therefore inhibition of Protocadherin Alpha Subfamily C, 2 (PCDHAC2, Accession NM_018899). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHAC2. CUG Triplet Repeat, RNA Binding Protein 2 (CUGBP2, Accession NM_006561) is another VGAM1474 host target gene. CUGBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUGBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUGBP2 BINDING SITE, designated SEQ ID:13332, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ

ID:4185.

[51198] Another function of VGAM1474 is therefore inhibition of CUG Triplet Repeat, RNA Binding Protein 2 (CUGBP2, Accession NM_006561). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CUGBP2. PRO2831 (Accession NM_018540) is another VGAM1474 host target gene. PRO2831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2831 BINDING SITE, designated SEQ ID:20611, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51199] Another function of VGAM1474 is therefore inhibition of PRO2831 (Accession NM_018540). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2831. LOC150577 (Accession XM_097918) is another VGAM1474 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC150577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41220, to the nucleotide sequence of VGAM1474 RNA, herein designated VGAM RNA, also designated SEQ ID:4185.

[51200] Another function of VGAM1474 is therefore inhibition of LOC150577 (Accession XM_097918). Accordingly, utilities of VGAM1474 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150577. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1475 (VGAM1475) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51201] VGAM1475 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1475 was detected is described hereinabove with reference to Figs. 1-8.

[51202] VGAM1475 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51203] VGAM1475 gene encodes a VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1475 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1475 precursor RNA is designated SEQ ID:1461, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1461 is located at position 3422 relative to the genome of Cocksfoot Streak Virus (CSV).

[51204] VGAM1475 precursor RNA folds onto itself, forming VGAM1475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51205] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1475 folded precursor RNA into VGAM1475 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM1475 RNA is designated SEQ ID:4186, and is provided hereinbelow with reference to the sequence listing part.

[51206] VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1475 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51207] VGAM1475 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1475 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1475 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51208] The complementary binding of VGAM1475 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1475 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1475

host target RNA into VGAM1475 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51209] It is appreciated that VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1475 host target genes. The mRNA of each one of this plurality of VGAM1475 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1475 RNA, herein designated VGAM RNA, and which when bound by VGAM1475 RNA causes inhibition of translation of respective one or more VGAM1475 host target proteins.

[51210] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1475 gene, herein designated VGAM GENE, on one or more VGAM1475 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51211] It is yet further appreciated that a function of VGAM1475 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1475 correlate with, and may be deduced from, the identity of the host target genes which VGAM1475 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51212] Nucleotide sequences of the VGAM1475 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1475 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1475 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1475 are further

described hereinbelow with reference to Table 1.

[51213] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1475 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1475 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51214] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1475 gene, herein designated VGAM is inhibition of expression of VGAM1475 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1475 correlate with, and may be deduced from, the identity of the target genes which VGAM1475 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51215] Thioredoxin Interacting Protein (TXNIP, Accession NM_006472) is a VGAM1475 host target gene. TXNIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TXNIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

TXNIP BINDING SITE, designated SEQ ID:13197, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51216] A function of VGAM1475 is therefore inhibition of Thioredoxin Interacting Protein (TXNIP, Accession NM_006472), a gene which binds and inhibits thioredoxin, a major regulator of cellular redox state. Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TXNIP. The function of TXNIP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM737. Zinc Finger Protein 215 (ZNF215, Accession NM_013250) is another VGAM1475 host target gene. ZNF215 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF215 BINDING SITE, designated SEQ ID:14913, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51217] Another function of VGAM1475 is therefore inhibition of Zinc Finger Protein 215 (ZNF215, Accession NM_013250). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF215. ARNTL2 (Accession NM_020183) is another VGAM1475 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21415, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51218] Another function of VGAM1475 is therefore inhibition of ARNTL2 (Accession NM_020183). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. BNIP-S (Accession NM_138278) is another VGAM1475 host target gene. BNIP-S BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BNIP-S, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNIP-S BINDING SITE, designated SEQ ID:28691, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51219] Another function of VGAM1475 is therefore inhibition of BNIP-S (Accession NM_138278). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNIP-S. DKFZP564D0764 (Accession XM_113964) is another VGAM1475 host target gene. DKFZP564D0764 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D0764, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D0764 BINDING SITE, designated SEQ ID:42575, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51220] Another function of VGAM1475 is therefore inhibition of DKFZP564D0764 (Accession XM_113964). Accordingly,

utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D0764. FLJ10352 (Accession NM_032142) is another VGAM1475 host target gene. FLJ10352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10352 BINDING SITE, designated SEQ ID:25825, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51221] Another function of VGAM1475 is therefore inhibition of FLJ10352 (Accession NM_032142). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10352. LOC120772 (Accession XM_058505) is another VGAM1475 host target gene. LOC120772 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC120772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC120772 BINDING SITE, designated SEQ ID:36629, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51222] Another function of VGAM1475 is therefore inhibition of LOC120772 (Accession XM_058505). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120772. LOC139767 (Accession XM_066883) is another VGAM1475 host target gene. LOC139767 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC139767, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139767 BINDING SITE, designated SEQ ID:37346, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51223] Another function of VGAM1475 is therefore inhibition of LOC139767 (Accession XM_066883). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139767. LOC154007 (Accession XM_087824) is another VGAM1475 host target gene. LOC154007 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154007 BINDING SITE, designated SEQ ID:39454, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51224] Another function of VGAM1475 is therefore inhibition of LOC154007 (Accession XM_087824). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154007. LOC256867 (Accession XM_170694) is another VGAM1475 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45475, to the nucleotide sequence of VGAM1475 RNA, herein designated VGAM RNA, also designated SEQ ID:4186.

[51225] Another function of VGAM1475 is therefore inhibition of

LOC256867 (Accession XM_170694). Accordingly, utilities of VGAM1475 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1476 (VGAM1476) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51226] VGAM1476 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1476 was detected is described hereinabove with reference to Figs. 1-8.

[51227] VGAM1476 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51228] VGAM1476 gene encodes a VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1476 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1476 precursor RNA is designated SEQ ID:1462, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1462 is located at position 7485 relative to the genome of Cocksfoot Streak Virus (CSV).

- [51229] VGAM1476 precursor RNA folds onto itself, forming VGAM1476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51230] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1476 folded precursor RNA into VGAM1476 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide se-

quence of VGAM1476 RNA is designated SEQ ID:4187, and is provided hereinbelow with reference to the sequence listing part.

[51231] VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1476 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51232] VGAM1476 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1476 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1476 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51233] The complementary binding of VGAM1476 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1476 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1476 host target RNA into VGAM1476 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51234] It is appreciated that VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1476 host target genes. The mRNA of each one of this plurality of VGAM1476 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1476 RNA, herein designated VGAM RNA, and which when bound by VGAM1476 RNA causes inhibition of translation of respective one or more VGAM1476 host target proteins.

[51235] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1476 gene, herein designated VGAM GENE, on one or more VGAM1476 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51236] It is yet further appreciated that a function of VGAM1476

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1476 correlate with, and may be deduced from, the identity of the host target genes which VGAM1476 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51237] Nucleotide sequences of the VGAM1476 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1476 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1476 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1476 are further described hereinbelow with reference to Table 1.

[51238] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1476 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1476 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51239] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1476 gene, herein designated VGAM is inhibition of expression of VGAM1476 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1476 correlate with, and may be deduced from, the identity of the target genes which VGAM1476 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51240] Chromosome 8 Open Reading Frame 14 (C8orf14, Accession NM_054029) is a VGAM1476 host target gene. C8orf14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C8orf14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf14 BINDING SITE, designated SEQ ID:27640, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51241] A function of VGAM1476 is therefore inhibition of Chromosome 8 Open Reading Frame 14 (C8orf14, Accession NM_054029). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with C8orf14. CXYorf1 (Accession XM_088704) is another VGAM1476 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39916, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51242] Another function of VGAM1476 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. FLJ31709 (Accession NM_144636) is another VGAM1476 host target gene. FLJ31709 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ31709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31709 BINDING SITE, designated SEQ ID:29458, to the nucleotide

sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51243] Another function of VGAM1476 is therefore inhibition of FLJ31709 (Accession NM_144636). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31709. Histidyl-tRNA Synthetase-like (HARSL, Accession NM_012208) is another VGAM1476 host target gene. HARSL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HARSL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HARSL BINDING SITE, designated SEQ ID:14510, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51244] Another function of VGAM1476 is therefore inhibition of Histidyl-tRNA Synthetase-like (HARSL, Accession NM_012208). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HARSL. KIAA0513 (Accession NM_014732) is another VGAM1476 host target

gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16356, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51245] Another function of VGAM1476 is therefore inhibition of KIAA0513 (Accession NM_014732). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. LOC166042 (Accession XM_093623) is another VGAM1476 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40198, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51246] Another function of VGAM1476 is therefore inhibition of LOC166042 (Accession XM_093623). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC200093 (Accession XM_032184) is another VGAM1476 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31607, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51247] Another function of VGAM1476 is therefore inhibition of LOC200093 (Accession XM_032184). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC91040 (Accession XM_035641) is another VGAM1476 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32326, to the nucleotide sequence of VGAM1476 RNA, herein designated VGAM RNA, also designated SEQ ID:4187.

[51248] Another function of VGAM1476 is therefore inhibition of LOC91040 (Accession XM_035641). Accordingly, utilities of VGAM1476 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1477 (VGAM1477) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51249] VGAM1477 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1477 was detected is described hereinabove with reference to Figs. 1–8.

[51250] VGAM1477 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cocksfoot Streak Virus (CSV). VGAM1477 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51251] VGAM1477 gene encodes a VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1477 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1477 precursor RNA is designated SEQ ID:1463, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1463 is located at position 5489 relative to the genome of Cocksfoot Streak Virus (CSV).

[51252] VGAM1477 precursor RNA folds onto itself, forming VGAM1477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51253] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1477 folded precursor RNA into VGAM1477

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 90%) nucleotide sequence of VGAM1477 RNA is designated SEQ ID:4188, and is provided hereinbelow with reference to the sequence listing part.

[51254] VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1477 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51255] VGAM1477 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1477 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1477 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51256] The complementary binding of VGAM1477 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1477 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1477 host target RNA into VGAM1477 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[51257] It is appreciated that VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1477 host target genes. The mRNA of each one of this plurality of VGAM1477 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1477 RNA, herein designated VGAM RNA, and which when bound by VGAM1477 RNA causes inhibition of translation of respective one or more VGAM1477 host target proteins.

[51258] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1477 gene, herein designated VGAM GENE, on one or more VGAM1477 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51259] It is yet further appreciated that a function of VGAM1477 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1477 include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGAM1477 correlate with, and may be deduced from, the identity of the host target genes which VGAM1477 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51260] Nucleotide sequences of the VGAM1477 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1477 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1477 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1477 are further described hereinbelow with reference to Table 1.

[51261] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1477 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1477 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51262] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1477 gene, herein designated VGAM is inhibition of expression of VGAM1477 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1477 correlate with, and may be deduced from, the identity of the target genes which VGAM1477 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51263] LAG1 Longevity Assurance Homolog 2 (*S. cerevisiae*) (LASS2, Accession XM_041889) is a VGAM1477 host target gene. LASS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASS2 BINDING SITE, designated SEQ ID:33621, to the nucleotide sequence of VGAM1477 RNA,

herein designated VGAM RNA, also designated SEQ ID:4188.

[51264] A function of VGAM1477 is therefore inhibition of LAG1 Longevity Assurance Homolog 2 (*S. cerevisiae*) (LASS2, Accession XM_041889). Accordingly, utilities of VGAM1477 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASS2. HEMK (Accession NM_016173) is another VGAM1477 host target gene. HEMK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEMK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEMK BINDING SITE, designated SEQ ID:18263, to the nucleotide sequence of VGAM1477 RNA, herein designated VGAM RNA, also designated SEQ ID:4188.

[51265] Another function of VGAM1477 is therefore inhibition of HEMK (Accession NM_016173). Accordingly, utilities of VGAM1477 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEMK. LOC145623 (Accession XM_096822) is another VGAM1477 host target gene. LOC145623 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC145623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145623 BINDING SITE, designated SEQ ID:40543, to the nucleotide sequence of VGAM1477 RNA, herein designated VGAM RNA, also designated SEQ ID:4188.

[51266] Another function of VGAM1477 is therefore inhibition of LOC145623 (Accession XM_096822). Accordingly, utilities of VGAM1477 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145623. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1478 (VGAM1478) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51267] VGAM1478 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1478 was detected is described hereinabove with reference to Figs. 1-8.

[51268] VGAM1478 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Brome Streak Mosaic Virus. VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51269] VGAM1478 gene encodes a VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1478 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1478 precursor RNA is designated SEQ ID:1464, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1464 is located at position 7727 relative to the genome of Brome Streak Mosaic Virus.

[51270] VGAM1478 precursor RNA folds onto itself, forming VGAM1478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51271] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1478 folded precursor RNA into VGAM1478 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM1478 RNA is designated SEQ ID:4189, and is provided hereinbelow with reference to the sequence listing part.

[51272] VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1478 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51273] VGAM1478 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1478 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1478 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51274] The complementary binding of VGAM1478 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1478 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1478

host target RNA into VGAM1478 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51275] It is appreciated that VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1478 host target genes. The mRNA of each one of this plurality of VGAM1478 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1478 RNA, herein designated VGAM RNA, and which when bound by VGAM1478 RNA causes inhibition of translation of respective one or more VGAM1478 host target proteins.

[51276] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1478 gene, herein designated VGAM GENE, on one or more VGAM1478 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51277] It is yet further appreciated that a function of VGAM1478 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1478 include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1478 correlate with, and may be deduced from, the identity of the host target genes which VGAM1478 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51278] Nucleotide sequences of the VGAM1478 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1478 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1478 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1478 are further

described hereinbelow with reference to Table 1.

[51279] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1478 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1478 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51280] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1478 gene, herein designated VGAM is inhibition of expression of VGAM1478 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1478 correlate with, and may be deduced from, the identity of the target genes which VGAM1478 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51281] FLJ12704 (Accession NM_024998) is a VGAM1478 host target gene. FLJ12704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12704 BINDING SITE,

designated SEQ ID:24563, to the nucleotide sequence of VGAM1478 RNA, herein designated VGAM RNA, also designated SEQ ID:4189.

[51282] A function of VGAM1478 is therefore inhibition of FLJ12704 (Accession NM_024998). Accordingly, utilities of VGAM1478 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12704. MEGF10 (Accession NM_032446) is another VGAM1478 host target gene. MEGF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEGF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF10 BINDING SITE, designated SEQ ID:26212, to the nucleotide sequence of VGAM1478 RNA, herein designated VGAM RNA, also designated SEQ ID:4189.

[51283] Another function of VGAM1478 is therefore inhibition of MEGF10 (Accession NM_032446). Accordingly, utilities of VGAM1478 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEGF10. LOC90133 (Accession XM_029323) is another VGAM1478 host target gene. LOC90133 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90133 BINDING SITE, designated SEQ ID:30867, to the nucleotide sequence of VGAM1478 RNA, herein designated VGAM RNA, also designated SEQ ID:4189.

[51284] Another function of VGAM1478 is therefore inhibition of LOC90133 (Accession XM_029323). Accordingly, utilities of VGAM1478 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90133. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1479 (VGAM1479) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51285] VGAM1479 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1479 was detected is described hereinabove with reference to Figs. 1-8.

[51286] VGAM1479 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Brome Streak Mosaic Virus. VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51287] VGAM1479 gene encodes a VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1479 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1479 precursor RNA is designated SEQ ID:1465, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1465 is located at position 2629 relative to the genome of Brome Streak Mosaic Virus.

[51288] VGAM1479 precursor RNA folds onto itself, forming VGAM1479 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[51289] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1479 folded precursor RNA into VGAM1479 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1479 RNA is designated SEQ ID:4190, and is provided hereinbelow with reference to the sequence listing part.

[51290] VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1479 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51291] VGAM1479 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1479 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1479 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1479 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51292] The complementary binding of VGAM1479 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1479 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1479 host target RNA into VGAM1479 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51293] It is appreciated that VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1479 host target genes. The mRNA of each one of this plurality of VGAM1479 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1479 RNA, herein designated VGAM RNA, and which when bound by VGAM1479 RNA causes inhibition of translation of respective one or more VGAM1479 host target proteins.

[51294] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1479 gene, herein designated VGAM GENE, on one or more VGAM1479 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51295] It is yet further appreciated that a function of VGAM1479 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1479 correlate with, and may be deduced from, the identity of the host target genes which VGAM1479 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51296] Nucleotide sequences of the VGAM1479 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1479 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1479 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1479 are further described hereinbelow with reference to Table 1.

[51297] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1479 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1479 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51298] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1479 gene, herein designated VGAM is inhibition of expression of VGAM1479 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1479 correlate with, and may be deduced from, the identity of the target genes which VGAM1479 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51299] FIBL-6 (Accession XM_053531) is a VGAM1479 host target gene. FIBL-6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FIBL-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FIBL-6 BINDING SITE, designated SEQ ID:36100, to the nucleotide sequence of VGAM1479 RNA, herein designated VGAM RNA, also designated SEQ ID:4190.

[51300] A function of VGAM1479 is therefore inhibition of FIBL-6 (Accession XM_053531). Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FIBL-6. KIAA1795 (Accession XM_050988) is another VGAM1479 host target gene. KIAA1795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1795 BINDING SITE, designated SEQ ID:35697, to the nucleotide sequence of VGAM1479 RNA, herein designated VGAM RNA, also designated SEQ ID:4190.

[51301] Another function of VGAM1479 is therefore inhibition of KIAA1795 (Accession XM_050988). Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1795. LOC91263 (Accession XM_037264) is another

VGAM1479 host target gene. LOC91263 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91263 BINDING SITE, designated SEQ ID:32594, to the nucleotide sequence of VGAM1479 RNA, herein designated VGAM RNA, also designated SEQ ID:4190.

[51302] Another function of VGAM1479 is therefore inhibition of LOC91263 (Accession XM_037264). Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91263. LOC92391 (Accession XM_044793) is another VGAM1479 host target gene. LOC92391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92391 BINDING SITE, designated SEQ ID:34270, to the nucleotide sequence of VGAM1479 RNA, herein designated VGAM RNA, also designated SEQ ID:4190.

[51303] Another function of VGAM1479 is therefore inhibition of LOC92391 (Accession XM_044793). Accordingly, utilities of VGAM1479 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92391. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1480 (VGAM1480) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51304] VGAM1480 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1480 was detected is described hereinabove with reference to Figs. 1–8.

[51305] VGAM1480 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Brome Streak Mosaic Virus. VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51306] VGAM1480 gene encodes a VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1480 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1480 precursor RNA is designated SEQ ID:1466, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1466 is located at position 9535 relative to the genome of Brome Streak Mosaic Virus.

[51307] VGAM1480 precursor RNA folds onto itself, forming VGAM1480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51308] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1480 folded precursor RNA into VGAM1480 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 86%) nucleotide sequence of VGAM1480 RNA is designated SEQ ID:4191, and is provided hereinbelow with reference to the sequence listing part.

[51309] VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1480 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[51310] VGAM1480 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1480 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1480 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51311] The complementary binding of VGAM1480 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1480 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1480 host target RNA into VGAM1480 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51312] It is appreciated that VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1480 host target genes. The mRNA of each one of this plurality of VGAM1480 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1480 RNA, herein designated VGAM RNA, and which when bound by VGAM1480 RNA causes inhibition of translation of respective one or more VGAM1480 host target proteins.

[51313] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1480 gene, herein designated VGAM GENE, on one or more VGAM1480 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51314] It is yet further appreciated that a function of VGAM1480 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1480 correlate with, and may be deduced from, the identity of the host target genes which VGAM1480 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51315] Nucleotide sequences of the VGAM1480 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1480 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1480 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1480 are further described hereinbelow with reference to Table 1.

[51316] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1480 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1480 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[51317] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1480 gene, herein designated VGAM is inhibition of expression of VGAM1480 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1480 correlate with, and may be deduced from, the identity of the target genes which VGAM1480 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51318] Dual Specificity Phosphatase 4 (DUSP4, Accession NM_057158) is a VGAM1480 host target gene. DUSP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DUSP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP4 BINDING SITE, designated SEQ ID:27666, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51319] A function of VGAM1480 is therefore inhibition of Dual Specificity Phosphatase 4 (DUSP4, Accession NM_057158), a gene which regulates mitogenic signal transduction. Accordingly, utilities of VGAM1480 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with DUSP4. The function of DUSP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM110. Neurexin 2 (NRXN2, Accession NM_138732) is another VGAM1480 host target gene. NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3, designated SEQ ID:28982, SEQ ID:28988 and SEQ ID:17466 respectively, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51320] Another function of VGAM1480 is therefore inhibition of Neurexin 2 (NRXN2, Accession NM_138732), a gene which may be involved in cell recognition, cell adhesion, and may mediate intracellular signaling. Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

NRXN2. The function of NRXN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.POM (POM121 homolog, rat) and ZP3 Fusion (POMZP3, Accession NM_012230) is another VGAM1480 host target gene. POMZP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by POMZP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMZP3 BINDING SITE, designated SEQ ID:14528, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51321] Another function of VGAM1480 is therefore inhibition of POM (POM121 homolog, rat) and ZP3 Fusion (POMZP3, Accession NM_012230). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMZP3. DKFZp434I099 (Accession NM_032269) is another VGAM1480 host target gene. DKFZp434I099 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp434I099,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434I099 BINDING SITE, designated SEQ ID:26016, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51322] Another function of VGAM1480 is therefore inhibition of DKFZp434I099 (Accession NM_032269). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434I099. KIAA0828 (Accession XM_088105) is another VGAM1480 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39511, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51323] Another function of VGAM1480 is therefore inhibition of KIAA0828 (Accession XM_088105). Accordingly, utilities

of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. MGC2452 (Accession NM_032644) is another VGAM1480 host target gene. MGC2452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2452 BINDING SITE, designated SEQ ID:26365, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51324] Another function of VGAM1480 is therefore inhibition of MGC2452 (Accession NM_032644). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. MGC4655 (Accession NM_033309) is another VGAM1480 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655

BINDING SITE, designated SEQ ID:27147, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51325] Another function of VGAM1480 is therefore inhibition of MGC4655 (Accession NM_033309). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. LOC145945 (Accession XM_096908) is another VGAM1480 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40630, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51326] Another function of VGAM1480 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC219513 (Accession XM_169166) is another VGAM1480 host target gene. LOC219513 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219513 BINDING SITE, designated SEQ ID:45290, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51327] Another function of VGAM1480 is therefore inhibition of LOC219513 (Accession XM_169166). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219513. LOC220021 (Accession XM_167814) is another VGAM1480 host target gene. LOC220021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220021 BINDING SITE, designated SEQ ID:44849, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51328] Another function of VGAM1480 is therefore inhibition of

LOC220021 (Accession XM_167814). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220021. LOC90918 (Accession XM_034863) is another VGAM1480 host target gene. LOC90918 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90918 BINDING SITE, designated SEQ ID:32176, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51329] Another function of VGAM1480 is therefore inhibition of LOC90918 (Accession XM_034863). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90918. LOC92340 (Accession XM_044426) is another VGAM1480 host target gene. LOC92340 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC92340 BINDING SITE, designated SEQ ID:34197, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51330] Another function of VGAM1480 is therefore inhibition of LOC92340 (Accession XM_044426). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92340. LOC93166 (Accession XM_049619) is another VGAM1480 host target gene. LOC93166 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93166 BINDING SITE, designated SEQ ID:35461, to the nucleotide sequence of VGAM1480 RNA, herein designated VGAM RNA, also designated SEQ ID:4191.

[51331] Another function of VGAM1480 is therefore inhibition of LOC93166 (Accession XM_049619). Accordingly, utilities of VGAM1480 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93166. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1481 (VGAM1481) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51332] VGAM1481 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1481 was detected is described hereinabove with reference to Figs. 1–8.

[51333] VGAM1481 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Brome Streak Mosaic Virus. VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51334] VGAM1481 gene encodes a VGAM1481 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1481 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1481 precursor RNA is designated SEQ ID:1467, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1467 is located at position 953 relative to the genome of Brome Streak Mosaic Virus.

[51335] VGAM1481 precursor RNA folds onto itself, forming VGAM1481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51336] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1481 folded precursor RNA into VGAM1481 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM1481 RNA is designated SEQ ID:4192, and is provided hereinbelow with reference to the sequence listing part.

[51337] VGAM1481 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1481 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51338] VGAM1481 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1481 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1481 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1481 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[51339] The complementary binding of VGAM1481 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1481 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1481 host target RNA into VGAM1481 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51340] It is appreciated that VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1481 host target genes. The mRNA of each one of this plurality of VGAM1481 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1481 RNA, herein designated VGAM RNA, and which when bound by VGAM1481 RNA causes inhibition of translation of respective one or more

VGAM1481 host target proteins.

[51341] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1481 gene, herein designated VGAM GENE, on one or more VGAM1481 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51342] It is yet further appreciated that a function of VGAM1481 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus.

Specific functions, and accordingly utilities, of VGAM1481 correlate with, and may be deduced from, the identity of the host target genes which VGAM1481 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51343] Nucleotide sequences of the VGAM1481 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1481 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1481 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1481 are further described hereinbelow with reference to Table 1.

[51344] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1481 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1481 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51345] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1481 gene, herein designated VGAM is inhibition of expression of VGAM1481 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1481 correlate with, and may be deduced from, the identity of the target genes which VGAM1481 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51346] Melanoma Antigen, Family A, 10 (MAGEA10, Accession NM_021048) is a VGAM1481 host target gene. MAGEA10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAGEA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGEA10 BINDING SITE, designated SEQ ID:22033, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51347] A function of VGAM1481 is therefore inhibition of Melanoma Antigen, Family A, 10 (MAGEA10, Accession NM_021048), a gene which may play a role in embryonal development and tumor transformation or aspects of tumor progression. Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGEA10. The function of MAGEA10 and its association with various diseases and

clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Phosphoribosyl Pyrophosphate Synthetase 2 (PRPS2, Accession NM_002765) is another VGAM1481 host target gene. PRPS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPS2 BINDING SITE, designated SEQ ID:8654, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51348] Another function of VGAM1481 is therefore inhibition of Phosphoribosyl Pyrophosphate Synthetase 2 (PRPS2, Accession NM_002765), a gene which generates the PRPP needed for initiation of purine biosynthesis. Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPS2. The function of PRPS2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM828. Dickkopf Homolog 2 (*Xenopus lae-*

vis) (DKK2, Accession NM_014421) is another VGAM1481 host target gene. DKK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKK2 BINDING SITE, designated SEQ ID:15774, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51349] Another function of VGAM1481 is therefore inhibition of Dickkopf Homolog 2 (*Xenopus laevis*) (DKK2, Accession NM_014421). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKK2. FLJ12838 (Accession NM_024641) is another VGAM1481 host target gene. FLJ12838 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12838 BINDING SITE, designated SEQ ID:23925, to the nucleotide sequence of VGAM1481 RNA,

herein designated VGAM RNA, also designated SEQ ID:4192.

[51350] Another function of VGAM1481 is therefore inhibition of FLJ12838 (Accession NM_024641). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12838. KIAA0781 (Accession XM_041314) is another VGAM1481 host target gene. KIAA0781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0781 BINDING SITE, designated SEQ ID:33498, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51351] Another function of VGAM1481 is therefore inhibition of KIAA0781 (Accession XM_041314). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0781. SEC8 (Accession NM_021807) is another VGAM1481 host target gene. SEC8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by SEC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC8 BINDING SITE, designated SEQ ID:22358, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51352] Another function of VGAM1481 is therefore inhibition of SEC8 (Accession NM_021807). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC8. SOX30 (Accession NM_007017) is another VGAM1481 host target gene. SOX30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX30 BINDING SITE, designated SEQ ID:13873, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51353] Another function of VGAM1481 is therefore inhibition of SOX30 (Accession NM_007017). Accordingly, utilities of

VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOX30. LOC144455 (Accession XM_084871) is another VGAM1481 host target gene. LOC144455 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144455, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144455 BINDING SITE, designated SEQ ID:37750, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51354] Another function of VGAM1481 is therefore inhibition of LOC144455 (Accession XM_084871). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144455. LOC145644 (Accession XM_035608) is another VGAM1481 host target gene. LOC145644 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145644 BINDING SITE, designated SEQ ID:32290, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51355] Another function of VGAM1481 is therefore inhibition of LOC145644 (Accession XM_035608). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145644. LOC200953 (Accession XM_117302) is another VGAM1481 host target gene. LOC200953 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200953, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200953 BINDING SITE, designated SEQ ID:43367, to the nucleotide sequence of VGAM1481 RNA, herein designated VGAM RNA, also designated SEQ ID:4192.

[51356] Another function of VGAM1481 is therefore inhibition of LOC200953 (Accession XM_117302). Accordingly, utilities of VGAM1481 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200953. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1482 (VGAM1482) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51357] VGAM1482 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1482 was detected is described hereinabove with reference to Figs. 1–8.

[51358] VGAM1482 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Brome Streak Mosaic Virus. VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51359] VGAM1482 gene encodes a VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1482 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1482 precursor RNA is designated SEQ ID:1468, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1468 is located at position 40 relative to the

genome of Brome Streak Mosaic Virus.

- [51360] VGAM1482 precursor RNA folds onto itself, forming VGAM1482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51361] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1482 folded precursor RNA into VGAM1482 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1482 RNA is designated SEQ ID:4193, and is provided hereinbelow with reference to the sequence listing part.
- [51362] VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1482 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51363] VGAM1482 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1482 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1482 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51364] The complementary binding of VGAM1482 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1482 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1482 host target RNA into VGAM1482 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51365] It is appreciated that VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1482 host target genes. The mRNA of each one of this plurality of VGAM1482 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1482 RNA, herein designated VGAM RNA, and which when bound by VGAM1482 RNA causes inhibition of translation of respective one or more VGAM1482 host target proteins.

[51366] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1482 gene, herein designated VGAM GENE, on one or more VGAM1482 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51367] It is yet further appreciated that a function of VGAM1482 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1482 include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1482

correlate with, and may be deduced from, the identity of the host target genes which VGAM1482 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51368] Nucleotide sequences of the VGAM1482 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1482 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1482 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1482 are further described hereinbelow with reference to Table 1.

[51369] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1482 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1482 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51370] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1482 gene, herein designated VGAM is inhibition of expression of VGAM1482 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1482 correlate with, and may be deduced

from, the identity of the target genes which VGAM1482 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51371] Centaurin, Gamma 1 (CENTG1, Accession NM_014770) is a VGAM1482 host target gene. CENTG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CENTG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTG1 BINDING SITE, designated SEQ ID:16565, to the nucleotide sequence of VGAM1482 RNA, herein designated VGAM RNA, also designated SEQ ID:4193.

[51372] A function of VGAM1482 is therefore inhibition of Centaurin, Gamma 1 (CENTG1, Accession NM_014770). Accordingly, utilities of VGAM1482 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTG1. FLJ11726 (Accession NM_024971) is another VGAM1482 host target gene. FLJ11726 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11726, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11726 BINDING SITE, designated SEQ ID:24524, to the nucleotide sequence of VGAM1482 RNA, herein designated VGAM RNA, also designated SEQ ID:4193.

[51373] Another function of VGAM1482 is therefore inhibition of FLJ11726 (Accession NM_024971). Accordingly, utilities of VGAM1482 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11726. LOC219731 (Accession XM_167596) is another VGAM1482 host target gene. LOC219731 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219731, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219731 BINDING SITE, designated SEQ ID:44716, to the nucleotide sequence of VGAM1482 RNA, herein designated VGAM RNA, also designated SEQ ID:4193.

[51374] Another function of VGAM1482 is therefore inhibition of LOC219731 (Accession XM_167596). Accordingly, utilities of VGAM1482 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC219731. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1483 (VGAM1483) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51375] VGAM1483 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1483 was detected is described hereinabove with reference to Figs. 1–8.

[51376] VGAM1483 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Brome Streak Mosaic Virus. VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51377] VGAM1483 gene encodes a VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1483 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1483 precursor RNA is designated SEQ ID:1469, and is provided hereinbelow with ref–

erence to the sequence listing part. Nucleotide sequence SEQ ID:1469 is located at position 7435 relative to the genome of Brome Streak Mosaic Virus.

- [51378] VGAM1483 precursor RNA folds onto itself, forming VGAM1483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51379] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1483 folded precursor RNA into VGAM1483 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM1483 RNA is designated SEQ ID:4194, and is provided hereinbelow with reference to the sequence listing part.

[51380] VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1483 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[51381] VGAM1483 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1483 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1483 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51382] The complementary binding of VGAM1483 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1483 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1483 host target RNA into VGAM1483 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51383] It is appreciated that VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1483 host target genes. The mRNA of each one of this plurality of VGAM1483 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1483 RNA, herein designated VGAM RNA, and which when bound by VGAM1483 RNA causes

inhibition of translation of respective one or more VGAM1483 host target proteins.

[51384] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1483 gene, herein designated VGAM GENE, on one or more VGAM1483 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51385] It is yet further appreciated that a function of VGAM1483 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1483 include diagnosis, prevention and

treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1483 correlate with, and may be deduced from, the identity of the host target genes which VGAM1483 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51386] Nucleotide sequences of the VGAM1483 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1483 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1483 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1483 are further described hereinbelow with reference to Table 1.

[51387] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1483 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1483 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51388] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1483 gene, herein designated VGAM is inhibition of expression of VGAM1483 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM1483 correlate with, and may be deduced from, the identity of the target genes which VGAM1483 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51389] Tumor Necrosis Factor (ligand) Superfamily, Member 15 (TNFSF15, Accession NM_005118) is a VGAM1483 host target gene. TNFSF15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF15 BINDING SITE, designated SEQ ID:11598, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51390] A function of VGAM1483 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 15 (TNFSF15, Accession NM_005118), a gene which acts as an autocrine factor to induce apoptosis in endothelial cells. Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF15. The function of TNFSF15

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM350. Von Hippel-Lindau Syndrome (VHL, Accession NM_000551) is another VGAM1483 host target gene. VHL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VHL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VHL BINDING SITE, designated SEQ ID:6156, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51391] Another function of VGAM1483 is therefore inhibition of Von Hippel-Lindau Syndrome (VHL, Accession NM_000551), a gene which may control rna stability through the selective degradation of rna-bound proteins. Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VHL. The function of VHL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM197.FLJ00060 (Accession

XM_028154) is another VGAM1483 host target gene. FLJ00060 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00060 BINDING SITE, designated SEQ ID:30625, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51392] Another function of VGAM1483 is therefore inhibition of FLJ00060 (Accession XM_028154). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00060. KIAA1678 (Accession XM_051221) is another VGAM1483 host target gene. KIAA1678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1678 BINDING SITE, designated SEQ ID:35786, to the nucleotide sequence of VGAM1483 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4194.

[51393] Another function of VGAM1483 is therefore inhibition of KIAA1678 (Accession XM_051221). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1678. LOC148508 (Accession XM_097478) is another VGAM1483 host target gene. LOC148508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148508 BINDING SITE, designated SEQ ID:40884, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51394] Another function of VGAM1483 is therefore inhibition of LOC148508 (Accession XM_097478). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148508. LOC222681 (Accession XM_167116) is another VGAM1483 host target gene. LOC222681 BINDING SITE1 through LOC222681 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA

encoded by LOC222681, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222681 BINDING SITE1 through LOC222681 BINDING SITE6, designated SEQ ID:44608, SEQ ID:44609, SEQ ID:44610, SEQ ID:44611, SEQ ID:44612 and SEQ ID:44613 respectively, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51395] Another function of VGAM1483 is therefore inhibition of LOC222681 (Accession XM_167116). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222681. LOC257507 (Accession XM_175204) is another VGAM1483 host target gene. LOC257507 BINDING SITE1 through LOC257507 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC257507, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257507 BINDING SITE1 through LOC257507 BINDING SITE6, designated SEQ ID:46675, SEQ ID:46676, SEQ ID:46677, SEQ ID:46678,

SEQ ID:46679 and SEQ ID:46730 respectively, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51396] Another function of VGAM1483 is therefore inhibition of LOC257507 (Accession XM_175204). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257507. LOC257625 (Accession XM_175267) is another VGAM1483 host target gene. LOC257625 BINDING SITE1 through LOC257625 BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC257625, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257625 BINDING SITE1 through LOC257625 BINDING SITE6, designated SEQ ID:46732, SEQ ID:46733, SEQ ID:46734, SEQ ID:46735, SEQ ID:8980 and SEQ ID:21253 respectively, to the nucleotide sequence of VGAM1483 RNA, herein designated VGAM RNA, also designated SEQ ID:4194.

[51397] Another function of VGAM1483 is therefore inhibition of LOC257625 (Accession XM_175267). Accordingly, utilities of VGAM1483 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC257625. DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM_005137) is another VGAM1485 host target gene. DGCR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGCR2 BINDING SITE, designated SEQ ID:11611, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51398] Another function of VGAM1485 is therefore inhibition of DiGeorge Syndrome Critical Region Gene 2 (DGCR2, Accession NM_005137), a gene which could intervene in cell-cell or cell-matrix interactions. Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGCR2. The function of DGCR2 has been established by previous studies. The DiGeorge syndrome (DGS; 188400) and velocardiofacial syndrome (VCFS; 192430) may present many clinical problems, including cardiac defects, hypoparathyroidism, T-cell immunodeficiency, and facial

dysmorphism. They are frequently associated with deletions within 22q11.2 (accounting in part for the designation CATCH22), but a number of cases have no detectable molecular defect of this region. Daw et al. (1996) stated that a number of single case reports with deletions of 10p suggested genetic heterogeneity of DGS. They compared the regions of hemizygosity in 4 patients with terminal deletions of 10p (1 patient with hypoparathyroidism and 3 with DGS) and 1 patient with VCFS and a large interstitial deletion. Fluorescence in situ hybridization (FISH) analysis demonstrated that these patients had overlapping deletions at the 10p13/10p14 boundary. A YAC contig spanning the shortest region of deletion overlap (SRO) was assembled and allowed the size of the SRO to be approximated to 2 Mb. As with deletions of 22q11, phenotypes varied considerably between affected patients. Daw et al. (1996) concluded that the results strongly support the hypothesis that haploinsufficiency of a gene or genes within 10p (DGS2 locus) can cause the DGS/VCFS spectrum of malformations. Lichtner et al. (2000) reported clinical and molecular deletion analysis of a patient described by Hasegawa et al. (1997) and a new case, both with the HDR phenotype: hypoparathyroidism, deafness, and renal dys-

plasia (OMIM Ref. No. 146255). They were found to have partial monosomy for 10p due to terminal deletions with breakpoints between D10S585 and D10S1720. By comparison with data previously published on patients with DiGeorge/velocardiofacial syndrome associated with 10p monosomy, Lichtner et al. (2000) concluded that this is a contiguous gene syndrome. Hemizygosity for a proximal region can cause cardiac defects and T cell deficiency; hemizygosity for a more distal region can cause hypoparathyroidism, sensorineural deafness, and renal dysplasia.

[51399] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51400] Daw, S. C. M.; Taylor, C.; Kraman, M.; Call, K.; Mao, J.; Schuffenhauer, S.; Meitinger, T.; Lipson, T.; Goodship, J.; Scambler, P. : A common region of 10p deleted in DiGeorge and velocardiofacial syndromes. *Nature Genet.* 13: 458–461, 1996. ; and

[51401] Lichtner, P.; Konig, R.; Hasegawa, T.; Van Esch, H.; Meitinger, T.; Schuffenhauer, S. : An HDR (hypoparathyroidism, deafness, renal dysplasia) syndrome locus maps distal to the DiGeorg.

[51402] Further studies establishing the function and utilities of DGCR2 are found in John Hopkins OMIM database record ID 601362, and in cited publications numbered 9515–9516, 481 and 9517 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutaminase (GLS, Accession NM_014905) is another VGAM1485 host target gene. GLS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GLS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLS BINDING SITE, designated SEQ ID:17107, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51403] Another function of VGAM1485 is therefore inhibition of Glutaminase (GLS, Accession NM_014905). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLS. Indolethylamine N-methyltransferase (INMT, Accession NM_006774) is another VGAM1485 host target gene. INMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

INMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INMT BINDING SITE, designated SEQ ID:13647, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51404] Another function of VGAM1485 is therefore inhibition of Indolethylamine N-methyltransferase (INMT, Accession NM_006774). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INMT. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12B (PPP1R12B, Accession NM_032104) is another VGAM1485 host target gene. PPP1R12B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R12B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R12B BINDING SITE, designated SEQ ID:25795, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51405] Another function of VGAM1485 is therefore inhibition of

Protein Phosphatase 1, Regulatory (inhibitor) Subunit 12B (PPP1R12B, Accession NM_032104). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R12B. Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM_003473) is another VGAM1485 host target gene. STAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAM BINDING SITE, designated SEQ ID:9540, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51406] Another function of VGAM1485 is therefore inhibition of Signal Transducing Adaptor Molecule (SH3 domain and ITAM motif) 1 (STAM, Accession NM_003473), a gene which is as an adaptor molecule involved in the downstream signaling of cytokine receptors. Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAM. The function of STAM and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM927.WTAP (Accession NM_004906) is another VGAM1485 host target gene. WTAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WTAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WTAP BINDING SITE, designated SEQ ID:11343, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51407] Another function of VGAM1485 is therefore inhibition of WTAP (Accession NM_004906), a gene which plays a role in both transcriptional and posttranscriptional regulation of certain cellular genes. Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WTAP. The function of WTAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM874.KIAA0121 (Accession XM_052386) is another VGAM1485 host target gene. KIAA0121 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0121 BINDING SITE, designated SEQ ID:35966, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51408] Another function of VGAM1485 is therefore inhibition of KIAA0121 (Accession XM_052386). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. KIAA0546 (Accession XM_049055) is another VGAM1485 host target gene. KIAA0546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0546 BINDING SITE, designated SEQ ID:35328, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51409] Another function of VGAM1485 is therefore inhibition of

KIAA0546 (Accession XM_049055). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0546. KIAA0903 (Accession XM_049251) is another VGAM1485 host target gene. KIAA0903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0903 BINDING SITE, designated SEQ ID:35368, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51410] Another function of VGAM1485 is therefore inhibition of KIAA0903 (Accession XM_049251). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0903. KIAA1580 (Accession XM_045271) is another VGAM1485 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34406, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51411] Another function of VGAM1485 is therefore inhibition of KIAA1580 (Accession XM_045271). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. LOC131000 (Accession XM_067145) is another VGAM1485 host target gene. LOC131000 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC131000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131000 BINDING SITE, designated SEQ ID:37348, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51412] Another function of VGAM1485 is therefore inhibition of LOC131000 (Accession XM_067145). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131000. LOC158434 (Accession XM_098939) is an-

other VGAM1485 host target gene. LOC158434 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158434 BINDING SITE, designated SEQ ID:41982, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51413] Another function of VGAM1485 is therefore inhibition of LOC158434 (Accession XM_098939). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158434. LOC90643 (Accession XM_033145) is another VGAM1485 host target gene. LOC90643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90643 BINDING SITE, designated SEQ ID:31851, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51414] Another function of VGAM1485 is therefore inhibition of LOC90643 (Accession XM_033145). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90643. LOC91813 (Accession XM_040862) is another VGAM1485 host target gene. LOC91813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE, designated SEQ ID:33395, to the nucleotide sequence of VGAM1485 RNA, herein designated VGAM RNA, also designated SEQ ID:4196.

[51415] Another function of VGAM1485 is therefore inhibition of LOC91813 (Accession XM_040862). Accordingly, utilities of VGAM1485 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1486 (VGAM1486) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[51416] VGAM1486 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1486 was detected is described hereinabove with reference to Figs. 1–8.

[51417] VGAM1486 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid Herpesvirus 2. VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51418] VGAM1486 gene encodes a VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1486 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1486 precursor RNA is designated SEQ ID:1472, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1472 is located at position 82050 relative to the genome of Gallid Herpesvirus 2.

[51419] VGAM1486 precursor RNA folds onto itself, forming VGAM1486 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51420] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1486 folded precursor RNA into VGAM1486 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1486 RNA is designated SEQ ID:4197, and is provided hereinbelow with reference to the sequence listing part.

[51421] VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1486 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51422] VGAM1486 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1486 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1486 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51423] The complementary binding of VGAM1486 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1486 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1486 host target RNA into VGAM1486 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51424] It is appreciated that VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1486 host target genes. The mRNA of each one of this plurality of VGAM1486 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1486 RNA, herein designated VGAM RNA, and which when bound by VGAM1486 RNA causes inhibition of translation of respective one or more VGAM1486 host target proteins.

[51425] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1486 gene, herein designated VGAM GENE, on one or more VGAM1486 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51426] It is yet further appreciated that a function of VGAM1486 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1486 include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1486 correlate with, and may be deduced from, the identity of the host target genes which VGAM1486 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[51427] Nucleotide sequences of the VGAM1486 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1486 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1486 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1486 are further described hereinbelow with reference to Table 1.

[51428] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1486 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1486 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51429] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1486 gene, herein designated VGAM is inhibition of expression of VGAM1486 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1486 correlate with, and may be deduced from, the identity of the target genes which VGAM1486 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51430] Promyelocytic Leukemia (PML, Accession NM_033238) is a VGAM1486 host target gene. PML BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PML, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE, designated SEQ ID:27077, to the nucleotide sequence of VGAM1486 RNA, herein designated VGAM RNA, also designated SEQ ID:4197.

[51431] A function of VGAM1486 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM_033238). Accordingly, utilities of VGAM1486 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. Zinc Finger Protein 192 (ZNF192, Accession NM_006298) is another VGAM1486 host target gene. ZNF192 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF192 BINDING SITE, designated SEQ ID:12987, to the nucleotide sequence of

VGAM1486 RNA, herein designated VGAM RNA, also designated SEQ ID:4197.

[51432] Another function of VGAM1486 is therefore inhibition of Zinc Finger Protein 192 (ZNF192, Accession NM_006298). Accordingly, utilities of VGAM1486 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF192. MGC14161 (Accession NM_032892) is another VGAM1486 host target gene. MGC14161 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC14161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14161 BINDING SITE, designated SEQ ID:26721, to the nucleotide sequence of VGAM1486 RNA, herein designated VGAM RNA, also designated SEQ ID:4197.

[51433] Another function of VGAM1486 is therefore inhibition of MGC14161 (Accession NM_032892). Accordingly, utilities of VGAM1486 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14161. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 1487 (VGAM1487) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51434] VGAM1487 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1487 was detected is described hereinabove with reference to Figs. 1–8.

[51435] VGAM1487 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Gallid Herpesvirus 2. VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51436] VGAM1487 gene encodes a VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1487 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1487 precursor RNA is designated SEQ ID:1473, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1473 is located at position 80281 relative to the

genome of Gallid Herpesvirus 2.

[51437] VGAM1487 precursor RNA folds onto itself, forming VGAM1487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51438] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1487 folded precursor RNA into VGAM1487 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1487 RNA is designated SEQ ID:4198, and is provided hereinbelow with reference to the sequence listing part.

[51439] VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1487 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51440] VGAM1487 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1487 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1487 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51441] The complementary binding of VGAM1487 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1487 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1487 host target RNA into VGAM1487 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51442] It is appreciated that VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1487 host target genes. The mRNA of each one of this plurality of VGAM1487 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1487 RNA, herein designated VGAM RNA, and which when bound by VGAM1487 RNA causes inhibition of translation of respective one or more VGAM1487 host target proteins.

[51443] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1487 gene, herein designated VGAM GENE, on one or more VGAM1487 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51444] It is yet further appreciated that a function of VGAM1487 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM1487

correlate with, and may be deduced from, the identity of the host target genes which VGAM1487 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51445] Nucleotide sequences of the VGAM1487 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1487 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1487 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1487 are further described hereinbelow with reference to Table 1.

[51446] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1487 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1487 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51447] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1487 gene, herein designated VGAM is inhibition of expression of VGAM1487 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1487 correlate with, and may be deduced

from, the identity of the target genes which VGAM1487 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51448] Development and Differentiation Enhancing Factor 2 (DDEF2, Accession NM_003887) is a VGAM1487 host target gene. DDEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDEF2 BINDING SITE, designated SEQ ID:9965, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51449] A function of VGAM1487 is therefore inhibition of Development and Differentiation Enhancing Factor 2 (DDEF2, Accession NM_003887), a gene which interacts with members of the Arf and Src family. Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDEF2. The function of DDEF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM464. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_002848) is another VGAM1487 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1 through PTPRO BINDING SITE5, designated SEQ ID:8738, SEQ ID:25018, SEQ ID:25027, SEQ ID:25003 and SEQ ID:25009 respectively, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51450] Another function of VGAM1487 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_002848), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM140.DKFZp762K2015 (Accession XM_051791) is another VGAM1487 host target gene. DKFZp762K2015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762K2015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762K2015 BINDING SITE, designated SEQ ID:35883, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51451] Another function of VGAM1487 is therefore inhibition of DKFZp762K2015 (Accession XM_051791). Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762K2015. FLJ21290 (Accession NM_025034) is another VGAM1487 host target gene. FLJ21290 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21290 BINDING SITE, designated SEQ ID:24631, to the

nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51452] Another function of VGAM1487 is therefore inhibition of FLJ21290 (Accession NM_025034). Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21290. IPLA2(GAMMA) (Accession XM_027224) is another VGAM1487 host target gene. IPLA2(GAMMA) BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IPLA2(GAMMA), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IPLA2(GAMMA) BINDING SITE, designated SEQ ID:30443, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51453] Another function of VGAM1487 is therefore inhibition of IPLA2(GAMMA) (Accession XM_027224). Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IPLA2(GAMMA). MGC11349 (Accession NM_025112) is another VGAM1487 host target gene. MGC11349 BIND-

ING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC11349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11349 BINDING SITE, designated SEQ ID:24759, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51454] Another function of VGAM1487 is therefore inhibition of MGC11349 (Accession NM_025112). Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11349. LOC219686 (Accession XM_165544) is another VGAM1487 host target gene. LOC219686 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219686 BINDING SITE, designated SEQ ID:43672, to the nucleotide sequence of VGAM1487 RNA, herein designated VGAM RNA, also designated SEQ ID:4198.

[51455] Another function of VGAM1487 is therefore inhibition of

LOC219686 (Accession XM_165544). Accordingly, utilities of VGAM1487 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219686. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1488 (VGAM1488) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51456] VGAM1488 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1488 was detected is described hereinabove with reference to Figs. 1-8.

[51457] VGAM1488 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plum Pox Virus.

VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51458] VGAM1488 gene encodes a VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1488 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1488 precursor RNA is designated SEQ ID:1474, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1474 is located at position 7567 relative to the genome of Plum Pox Virus.

- [51459] VGAM1488 precursor RNA folds onto itself, forming VGAM1488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51460] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1488 folded precursor RNA into VGAM1488 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide se-

quence of VGAM1488 RNA is designated SEQ ID:4199, and is provided hereinbelow with reference to the sequence listing part.

[51461] VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1488 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51462] VGAM1488 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1488 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1488 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51463] The complementary binding of VGAM1488 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1488 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1488 host target RNA into VGAM1488 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51464] It is appreciated that VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1488 host target genes. The mRNA of each one of this plurality of VGAM1488 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1488 RNA, herein designated VGAM RNA, and which when bound by VGAM1488 RNA causes inhibition of translation of respective one or more VGAM1488 host target proteins.

[51465] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1488 gene, herein designated VGAM GENE, on one or more VGAM1488 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51466] It is yet further appreciated that a function of VGAM1488

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of viral infection by Plum Pox Virus. Specific functions, and accordingly utilities, of VGAM1488 correlate with, and may be deduced from, the identity of the host target genes which VGAM1488 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51467] Nucleotide sequences of the VGAM1488 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1488 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1488 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1488 are further described hereinbelow with reference to Table 1.

[51468] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1488 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1488 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51469] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1488 gene, herein designated VGAM is inhibition of expression of VGAM1488 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1488 correlate with, and may be deduced from, the identity of the target genes which VGAM1488 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51470] A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM_139275) is a VGAM1488 host target gene. AKAP1 BINDING SITE1 and AKAP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AKAP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP1 BINDING SITE1 and AKAP1 BINDING SITE2, designated SEQ ID:29267 and SEQ ID:9581 respectively, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51471] A function of VGAM1488 is therefore inhibition of A Kinase (PRKA) Anchor Protein 1 (AKAP1, Accession NM_139275), a gene which binds to type i and ii regula-

tory subunits of protein kinase a . Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP1. The function of AKAP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1392.Cysteine-rich, Angiogenic Inducer, 61 (CYR61, Accession NM_001554) is another VGAM1488 host target gene. CYR61 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CYR61, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYR61 BINDING SITE, designated SEQ ID:7277, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51472] Another function of VGAM1488 is therefore inhibition of Cysteine-rich, Angiogenic Inducer, 61 (CYR61, Accession NM_001554), a gene which promotes the adhesion of endothelial cells . Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYR61. The function of

CYR61 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1229.F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM_012158) is another VGAM1488 host target gene. FBXL3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL3A BINDING SITE, designated SEQ ID:14457, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51473] Another function of VGAM1488 is therefore inhibition of F-box and Leucine-rich Repeat Protein 3A (FBXL3A, Accession NM_012158), a gene which is a putative SCF ubiquitin ligase subunit involved in protein degradation. Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL3A. The function of FBXL3A and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM1172.Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_002941) is another VGAM1488 host target gene. ROBO1 BINDING SITE1 and ROBO1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ROBO1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO1 BINDING SITE1 and ROBO1 BINDING SITE2, designated SEQ ID:8847 and SEQ ID:28582 respectively, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51474] Another function of VGAM1488 is therefore inhibition of Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_002941), a gene which is an axon guidance receptor. Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO1. The function of ROBO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM37.T-complex-associated-testis-expressed 1-like (TCTE1L, Accession XM_048205) is another VGAM1488 host target gene. TCTE1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCTE1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCTE1L BINDING SITE, designated SEQ ID:35144, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51475] Another function of VGAM1488 is therefore inhibition of T-complex-associated-testis-expressed 1-like (TCTE1L, Accession XM_048205). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCTE1L. Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916) is another VGAM1488 host target gene. AP1S2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of AP1S2 BINDING SITE, designated SEQ ID:10004, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51476] Another function of VGAM1488 is therefore inhibition of Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1S2. Apoptosis Inhibitor 5 (API5, Accession NM_006595) is another VGAM1488 host target gene. API5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by API5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of API5 BINDING SITE, designated SEQ ID:13364, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51477] Another function of VGAM1488 is therefore inhibition of Apoptosis Inhibitor 5 (API5, Accession NM_006595). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with API5. CGI-57 (Accession XM_058098) is another VGAM1488 host target gene. CGI-57 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGI-57, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-57 BINDING SITE, designated SEQ ID:36575, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51478] Another function of VGAM1488 is therefore inhibition of CGI-57 (Accession XM_058098). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-57. DKFZp434A2417 (Accession XM_038526) is another VGAM1488 host target gene. DKFZp434A2417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434A2417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434A2417 BINDING SITE, designated SEQ ID:32864, to the nucleotide sequence of VGAM1488

RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51479] Another function of VGAM1488 is therefore inhibition of DKFZp434A2417 (Accession XM_038526). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434A2417. FLJ12488 (Accession NM_031218) is another VGAM1488 host target gene. FLJ12488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12488 BINDING SITE, designated SEQ ID:25265, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51480] Another function of VGAM1488 is therefore inhibition of FLJ12488 (Accession NM_031218). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12488. KIAA0633 (Accession XM_168380) is another VGAM1488 host target gene. KIAA0633 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0633, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0633 BINDING SITE, designated SEQ ID:45142, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51481] Another function of VGAM1488 is therefore inhibition of KIAA0633 (Accession XM_168380). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0633. KIAA0794 (Accession XM_087353) is another VGAM1488 host target gene. KIAA0794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0794 BINDING SITE, designated SEQ ID:39188, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51482] Another function of VGAM1488 is therefore inhibition of KIAA0794 (Accession XM_087353). Accordingly, utilities

of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0794. KIAA0924 (Accession NM_014897) is another VGAM1488 host target gene. KIAA0924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0924 BINDING SITE, designated SEQ ID:17068, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51483] Another function of VGAM1488 is therefore inhibition of KIAA0924 (Accession NM_014897). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0924. KIAA1430 (Accession XM_087593) is another VGAM1488 host target gene. KIAA1430 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1430 BINDING SITE, designated SEQ ID:39359, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51484] Another function of VGAM1488 is therefore inhibition of KIAA1430 (Accession XM_087593). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1430. KIAA1495 (Accession XM_055080) is another VGAM1488 host target gene. KIAA1495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1495 BINDING SITE, designated SEQ ID:36226, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51485] Another function of VGAM1488 is therefore inhibition of KIAA1495 (Accession XM_055080). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1495. PGR1 (Accession NM_033296) is another VGAM1488 host target gene. PGR1 BINDING SITE is HOST

TARGET binding site found in the 3` untranslated region of mRNA encoded by PGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGR1 BINDING SITE, designated SEQ ID:27125, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51486] Another function of VGAM1488 is therefore inhibition of PGR1 (Accession NM_033296). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGR1. PRO1635 (Accession NM_018589) is another VGAM1488 host target gene. PRO1635 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRO1635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1635 BINDING SITE, designated SEQ ID:20668, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51487] Another function of VGAM1488 is therefore inhibition of

PRO1635 (Accession NM_018589). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1635. SMAP1 (Accession NM_021940) is another VGAM1488 host target gene. SMAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMAP1 BINDING SITE, designated SEQ ID:22456, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51488] Another function of VGAM1488 is therefore inhibition of SMAP1 (Accession NM_021940). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMAP1. LOC158427 (Accession NM_139246) is another VGAM1488 host target gene. LOC158427 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC158427 BINDING SITE, designated SEQ ID:29245, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51489] Another function of VGAM1488 is therefore inhibition of LOC158427 (Accession NM_139246). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158427. LOC163231 (Accession XM_092094) is another VGAM1488 host target gene. LOC163231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163231 BINDING SITE, designated SEQ ID:40097, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51490] Another function of VGAM1488 is therefore inhibition of LOC163231 (Accession XM_092094). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163231. LOC205251 (Accession XM_119554) is an-

other VGAM1488 host target gene. LOC205251 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205251 BINDING SITE, designated SEQ ID:43588, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51491] Another function of VGAM1488 is therefore inhibition of LOC205251 (Accession XM_119554). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205251. LOC220018 (Accession XM_167816) is another VGAM1488 host target gene. LOC220018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220018 BINDING SITE, designated SEQ ID:44858, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51492] Another function of VGAM1488 is therefore inhibition of LOC220018 (Accession XM_167816). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220018. LOC51336 (Accession NM_016646) is another VGAM1488 host target gene. LOC51336 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51336 BINDING SITE, designated SEQ ID:18759, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51493] Another function of VGAM1488 is therefore inhibition of LOC51336 (Accession NM_016646). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51336. LOC91266 (Accession XM_037268) is another VGAM1488 host target gene. LOC91266 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91266, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91266 BINDING SITE, designated SEQ ID:32603, to the nucleotide sequence of VGAM1488 RNA, herein designated VGAM RNA, also designated SEQ ID:4199.

[51494] Another function of VGAM1488 is therefore inhibition of LOC91266 (Accession XM_037268). Accordingly, utilities of VGAM1488 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91266. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1489 (VGAM1489) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51495] VGAM1489 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1489 was detected is described hereinabove with reference to Figs. 1-8.

[51496] VGAM1489 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plum Pox Virus. VGAM1489 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[51497] VGAM1489 gene encodes a VGAM1489 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1489 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1489 precursor RNA is designated SEQ ID:1475, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1475 is located at position 8790 relative to the genome of Plum Pox Virus.

[51498] VGAM1489 precursor RNA folds onto itself, forming VGAM1489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51499] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1489 folded precursor RNA into VGAM1489

RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM1489 RNA is designated SEQ ID:4200, and is provided hereinbelow with reference to the sequence listing part.

[51500] VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1489 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51501] VGAM1489 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1489 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1489 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51502] The complementary binding of VGAM1489 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1489 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1489 host target RNA into VGAM1489 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM

host target protein is therefore outlined by a broken line.

[51503] It is appreciated that VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1489 host target genes. The mRNA of each one of this plurality of VGAM1489 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1489 RNA, herein designated VGAM RNA, and which when bound by VGAM1489 RNA causes inhibition of translation of respective one or more VGAM1489 host target proteins.

[51504] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1489 gene, herein designated VGAM GENE, on one or more VGAM1489 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51505] It is yet further appreciated that a function of VGAM1489 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of viral infection by Plum Pox Virus. Specific functions, and accordingly utilities, of VGAM1489 correlate with, and may be deduced from, the identity of the host target genes which VGAM1489 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51506] Nucleotide sequences of the VGAM1489 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1489 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1489 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1489 are further described hereinbelow with reference to Table 1.

[51507] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1489 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1489 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51508] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1489 gene, herein designated VGAM is inhibition of expression of VGAM1489 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1489 correlate with, and may be deduced from, the identity of the target genes which VGAM1489 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51509] IL2-inducible T-cell Kinase (ITK, Accession NM_005546) is a VGAM1489 host target gene. ITK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITK BINDING SITE, designated SEQ ID:12077, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4200.

[51510] A function of VGAM1489 is therefore inhibition of IL2-inducible T-cell Kinase (ITK, Accession NM_005546), a gene which plays a role in t cell proliferation and differentiation. Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITK. The function of ITK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM288. Keratin, Hair, Acidic, 8 (KRTHA8, Accession NM_006771) is another VGAM1489 host target gene. KRTHA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KRTHA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KRTHA8 BINDING SITE, designated SEQ ID:13645, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51511] Another function of VGAM1489 is therefore inhibition of Keratin, Hair, Acidic, 8 (KRTHA8, Accession NM_006771), a gene which a type I keratin that may form intermediate

filaments. Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KRTHA8. The function of KRTHA8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM910. TEM8 (Accession NM_032208) is another VGAM1489 host target gene. TEM8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM8 BINDING SITE, designated SEQ ID:25918, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51512] Another function of VGAM1489 is therefore inhibition of TEM8 (Accession NM_032208), a gene which is a tumor-specific endothelial marker. Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM8. The function of TEM8 has been established by previous studies. St. Croix et al. (2000) compared gene expression

patterns of endothelial cells derived from blood vessels of normal and malignant colorectal tissues to identify genes involved in tumor angiogenesis. Among the genes they identified was TEM8, which encodes a 564-amino acid protein. Bradley et al. (2001) isolated a cDNA encoding ATR and determined that the first 364 amino acids of the 368-amino acid ATR protein are identical to those of TEM8. The C-terminal ends of the ATR and TEM8 proteins then diverge, presumably due to alternative splicing, such that ATR has a cytoplasmic tail of only 25 amino acids, whereas TEM8 has a cytoplasmic tail of 221 amino acids. (Bradley et al. (2001) noted in proof that another apparently full-length ATR/TEM8-related cDNA clone (GenBank BC01207) encodes a protein with yet another C-terminal end.) The ATR protein contains a 27-amino acid signal peptide; a 293-amino acid extracellular domain with 3 putative end-length glycosylation sites; and a 23-amino acid putative transmembrane region followed by the short cytoplasmic tail. An extracellular von Willebrand factor type A (VWA) domain is located between residues 44 and 216 of the ATR protein. The cytoplasmic tail of ATR contains an acidic cluster (EESEE) similar to a motif in the cytoplasmic tail of furin (OMIM Ref. No. 136950) that speci-

fies basolateral sorting of this protease in polarized epithelial cells. The mouse homolog of ATR/TEM8 is highly related to the human clones, showing more than 98% sequence identity in the extracellular domain. ATR and/or TEM8 is expressed in a number of different tissues, including central nervous system, heart, lung, and lymphocytes. Bradley et al. (2001) confirmed that the VWA domain of ATR binds directly to the protective antigen of anthrax, suggesting that ATR may also function as a protective antigen receptor. They suggested that the finding that the soluble VWA domain of ATR inhibits toxin action, coupled with the use of the cloned receptor as a tool for identifying inhibitors of the protective antigen-receptor interaction, holds promise for the development of novel approaches for the treatment of anthrax.

[51513] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51514] St. Croix, B.; Rago, C.; Velculescu, V.; Traverso, G.; Romans, K. E.; Montgomery, E.; Lal, A.; Riggins, G. J.; Lengauer, C.; Vogelstein, B.; Kinzler, K. W. : Genes expressed in human tumor endothelium. Science 289: 1197-1202, 2000. ; and

- [51515] Bradley, K. A.; Mogridge, J.; Mourez, M.; Collier, R. J.; Young, J. A. T. : Identification of the cellular receptor for anthrax toxin. *Nature* 414: 160–161, 2001.
- [51516] Further studies establishing the function and utilities of TEM8 are found in John Hopkins OMIM database record ID 606410, and in cited publications numbered 4533, 689 and 6907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BC022889 (Accession XM_096964) is another VGAM1489 host target gene. BC022889 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BC022889, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BC022889 BINDING SITE, designated SEQ ID:40684, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.
- [51517] Another function of VGAM1489 is therefore inhibition of BC022889 (Accession XM_096964). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BC022889. FLJ20546 (Accession NM_017872) is another

VGAM1489 host target gene. FLJ20546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20546 BINDING SITE, designated SEQ ID:19544, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51518] Another function of VGAM1489 is therefore inhibition of FLJ20546 (Accession NM_017872). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20546. FLJ20671 (Accession NM_017924) is another VGAM1489 host target gene. FLJ20671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20671 BINDING SITE, designated SEQ ID:19592, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51519] Another function of VGAM1489 is therefore inhibition of FLJ20671 (Accession NM_017924). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20671. FLJ23121 (Accession NM_024694) is another VGAM1489 host target gene. FLJ23121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23121 BINDING SITE, designated SEQ ID:24002, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51520] Another function of VGAM1489 is therefore inhibition of FLJ23121 (Accession NM_024694). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23121. KIAA1877 (Accession XM_038616) is another VGAM1489 host target gene. KIAA1877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1877, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1877 BINDING SITE, designated SEQ ID:32882, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51521] Another function of VGAM1489 is therefore inhibition of KIAA1877 (Accession XM_038616). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1877. MGC20470 (Accession NM_145053) is another VGAM1489 host target gene. MGC20470 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20470 BINDING SITE, designated SEQ ID:29686, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51522] Another function of VGAM1489 is therefore inhibition of MGC20470 (Accession NM_145053). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC20470. MGC4400 (Accession NM_032679) is another VGAM1489 host target gene. MGC4400 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4400 BINDING SITE, designated SEQ ID:26400, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51523] Another function of VGAM1489 is therefore inhibition of MGC4400 (Accession NM_032679). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4400. NLI-IF (Accession NM_021198) is another VGAM1489 host target gene. NLI-IF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NLI-IF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NLI-IF BINDING SITE, designated SEQ ID:22174, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4200.

[51524] Another function of VGAM1489 is therefore inhibition of NLI-IF (Accession NM_021198). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NLI-IF. Spir-2 (Accession XM_047462) is another VGAM1489 host target gene. Spir-2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by Spir-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Spir-2 BINDING SITE, designated SEQ ID:34964, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51525] Another function of VGAM1489 is therefore inhibition of Spir-2 (Accession XM_047462). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Spir-2. LOC120856 (Accession XM_058509) is another VGAM1489 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC120856, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36640, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51526] Another function of VGAM1489 is therefore inhibition of LOC120856 (Accession XM_058509). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120856. LOC143916 (Accession XM_084664) is another VGAM1489 host target gene. LOC143916 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143916 BINDING SITE, designated SEQ ID:37651, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51527] Another function of VGAM1489 is therefore inhibition of LOC143916 (Accession XM_084664). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC143916. LOC146506 (Accession XM_085489) is another VGAM1489 host target gene. LOC146506 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146506 BINDING SITE, designated SEQ ID:38180, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51528] Another function of VGAM1489 is therefore inhibition of LOC146506 (Accession XM_085489). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146506. LOC152316 (Accession XM_098185) is another VGAM1489 host target gene. LOC152316 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152316, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152316 BINDING SITE, designated SEQ ID:41453, to

the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51529] Another function of VGAM1489 is therefore inhibition of LOC152316 (Accession XM_098185). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152316. LOC169026 (Accession XM_095471) is another VGAM1489 host target gene. LOC169026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169026 BINDING SITE, designated SEQ ID:40266, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51530] Another function of VGAM1489 is therefore inhibition of LOC169026 (Accession XM_095471). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169026. LOC221876 (Accession XM_168220) is another VGAM1489 host target gene. LOC221876 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC221876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221876 BINDING SITE, designated SEQ ID:45078, to the nucleotide sequence of VGAM1489 RNA, herein designated VGAM RNA, also designated SEQ ID:4200.

[51531] Another function of VGAM1489 is therefore inhibition of LOC221876 (Accession XM_168220). Accordingly, utilities of VGAM1489 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221876. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1490 (VGAM1490) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51532] VGAM1490 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1490 was detected is described hereinabove with reference to Figs. 1-8.

[51533] VGAM1490 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Plum Pox Virus.

VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51534] VGAM1490 gene encodes a VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1490 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1490 precursor RNA is designated SEQ ID:1476, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1476 is located at position 5866 relative to the genome of Plum Pox Virus.

[51535] VGAM1490 precursor RNA folds onto itself, forming VGAM1490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51536] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1490 folded precursor RNA into VGAM1490 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM1490 RNA is designated SEQ ID:4201, and is provided hereinbelow with reference to the sequence listing part.

[51537] VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1490 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51538] VGAM1490 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM1490 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1490 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51539] The complementary binding of VGAM1490 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1490 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1490

host target RNA into VGAM1490 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51540] It is appreciated that VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1490 host target genes. The mRNA of each one of this plurality of VGAM1490 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1490 RNA, herein designated VGAM RNA, and which when bound by VGAM1490 RNA causes inhibition of translation of respective one or more VGAM1490 host target proteins.

[51541] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1490 gene, herein designated VGAM GENE, on one or more VGAM1490 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51542] It is yet further appreciated that a function of VGAM1490 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1490 include diagnosis, prevention and treatment of viral infection by Plum Pox Virus. Specific functions, and accordingly utilities, of VGAM1490 correlate with, and may be deduced from, the identity of the host target genes which VGAM1490 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51543] Nucleotide sequences of the VGAM1490 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1490 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1490 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1490 are further

described hereinbelow with reference to Table 1.

[51544] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1490 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1490 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51545] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1490 gene, herein designated VGAM is inhibition of expression of VGAM1490 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1490 correlate with, and may be deduced from, the identity of the target genes which VGAM1490 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51546] FLJ13187 (Accession NM_024613) is a VGAM1490 host target gene. FLJ13187 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13187 BINDING SITE,

designated SEQ ID:23869, to the nucleotide sequence of VGAM1490 RNA, herein designated VGAM RNA, also designated SEQ ID:4201.

[51547] A function of VGAM1490 is therefore inhibition of FLJ13187 (Accession NM_024613). Accordingly, utilities of VGAM1490 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13187. PLU-1 (Accession NM_006618) is another VGAM1490 host target gene. PLU-1 BINDING SITE1 and PLU-1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PLU-1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLU-1 BINDING SITE1 and PLU-1 BINDING SITE2, designated SEQ ID:13400 and SEQ ID:42249 respectively, to the nucleotide sequence of VGAM1490 RNA, herein designated VGAM RNA, also designated SEQ ID:4201.

[51548] Another function of VGAM1490 is therefore inhibition of PLU-1 (Accession NM_006618). Accordingly, utilities of VGAM1490 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLU-1.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1491 (VGAM1491) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51549] VGAM1491 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1491 was detected is described hereinabove with reference to Figs. 1–8.

[51550] VGAM1491 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plum Pox Virus. VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51551] VGAM1491 gene encodes a VGAM1491 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1491 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1491 precursor RNA is designated SEQ ID:1477, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence

SEQ ID:1477 is located at position 5456 relative to the genome of Plum Pox Virus.

[51552] VGAM1491 precursor RNA folds onto itself, forming VGAM1491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51553] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1491 folded precursor RNA into VGAM1491 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM1491 RNA is designated SEQ ID:4202, and is provided hereinbelow with reference to the sequence listing part.

[51554] VGAM1491 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1491 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51555] VGAM1491 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1491 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1491 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1491 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[51556] The complementary binding of VGAM1491 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1491 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1491 host target RNA into VGAM1491 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51557] It is appreciated that VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1491 host target genes. The mRNA of each one of this plurality of VGAM1491 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1491 RNA, herein designated VGAM RNA, and which when bound by VGAM1491 RNA causes inhibition of translation of respective one or more

VGAM1491 host target proteins.

[51558] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1491 gene, herein designated VGAM GENE, on one or more VGAM1491 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51559] It is yet further appreciated that a function of VGAM1491 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of viral infection by Plum Pox Virus. Specific

functions, and accordingly utilities, of VGAM1491 correlate with, and may be deduced from, the identity of the host target genes which VGAM1491 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51560] Nucleotide sequences of the VGAM1491 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1491 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1491 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1491 are further described hereinbelow with reference to Table 1.

[51561] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1491 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1491 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51562] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1491 gene, herein designated VGAM is inhibition of expression of VGAM1491 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM1491 correlate with, and may be deduced from, the identity of the target genes which VGAM1491 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51563] Immunoglobulin Superfamily Containing Leucine-rich Repeat (ISLR, Accession NM_005545) is a VGAM1491 host target gene. ISLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ISLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ISLR BINDING SITE, designated SEQ ID:12072, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51564] A function of VGAM1491 is therefore inhibition of Immunoglobulin Superfamily Containing Leucine-rich Repeat (ISLR, Accession NM_005545). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ISLR. SON DNA Binding Protein (SON, Accession NM_058183) is another VGAM1491 host target gene. SON BINDING SITE1 through SON BINDING SITE3 are HOST TARGET binding

sites found in untranslated regions of mRNA encoded by SON, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SON BINDING SITE1 through SON BINDING SITE3, designated SEQ ID:27743, SEQ ID:29039 and SEQ ID:29044 respectively, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51565] Another function of VGAM1491 is therefore inhibition of SON DNA Binding Protein (SON, Accession NM_058183). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SON. DKFZP572C163 (Accession XM_028314) is another VGAM1491 host target gene. DKFZP572C163 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP572C163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP572C163 BINDING SITE, designated SEQ ID:30655, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4202.

[51566] Another function of VGAM1491 is therefore inhibition of DKFZP572C163 (Accession XM_028314). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP572C163. KIAA0416 (Accession NM_015564) is another VGAM1491 host target gene. KIAA0416 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0416 BINDING SITE, designated SEQ ID:17829, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51567] Another function of VGAM1491 is therefore inhibition of KIAA0416 (Accession NM_015564). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0416. MASA (Accession XM_035994) is another VGAM1491 host target gene. MASA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MASA, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MASA BINDING SITE, designated SEQ ID:32372, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51568] Another function of VGAM1491 is therefore inhibition of MASA (Accession XM_035994). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MASA. LOC152065 (Accession XM_098159) is another VGAM1491 host target gene. LOC152065 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152065 BINDING SITE, designated SEQ ID:41430, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51569] Another function of VGAM1491 is therefore inhibition of LOC152065 (Accession XM_098159). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152065. LOC220766 (Accession XM_165471) is another VGAM1491 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220766 BINDING SITE, designated SEQ ID:43652, to the nucleotide sequence of VGAM1491 RNA, herein designated VGAM RNA, also designated SEQ ID:4202.

[51570] Another function of VGAM1491 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM1491 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1492 (VGAM1492) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51571] VGAM1492 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1492 was detected is described hereinabove with reference to Figs. 1–8.

[51572] VGAM1492 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Johnsongrass Mosaic Virus. VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51573] VGAM1492 gene encodes a VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1492 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1492 precursor RNA is designated SEQ ID:1478, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1478 is located at position 2047 relative to the genome of Johnsongrass Mosaic Virus.

[51574] VGAM1492 precursor RNA folds onto itself, forming VGAM1492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51575] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1492 folded precursor RNA into VGAM1492 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM1492 RNA is designated SEQ ID:4203, and is provided hereinbelow with reference to the sequence listing part.

[51576] VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1492 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51577] VGAM1492 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1492 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1492 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51578] The complementary binding of VGAM1492 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1492 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1492 host target RNA into VGAM1492 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51579] It is appreciated that VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1492 host target genes. The mRNA of each one of this plurality of VGAM1492 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1492 RNA, herein designated VGAM RNA, and which when bound by VGAM1492 RNA causes inhibition of translation of respective one or more VGAM1492 host target proteins.

[51580] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1492 gene, herein designated VGAM GENE, on one or more VGAM1492 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51581] It is yet further appreciated that a function of VGAM1492 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of viral infection by Johnsongrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1492 correlate with, and may be deduced from, the identity of the host target genes which VGAM1492 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51582] Nucleotide sequences of the VGAM1492 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1492 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1492 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1492 are further described hereinbelow with reference to Table 1.

[51583] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1492 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1492 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51584] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1492 gene, herein designated VGAM is inhibition of expression of VGAM1492 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1492 correlate with, and may be deduced from, the identity of the target genes which VGAM1492 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51585] CDC23 (cell division cycle 23, yeast, homolog) (CDC23, Accession NM_004661) is a VGAM1492 host target gene. CDC23 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by CDC23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC23 BINDING SITE, designated SEQ ID:11031, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51586] A function of VGAM1492 is therefore inhibition of CDC23 (cell division cycle 23, yeast, homolog) (CDC23, Accession NM_004661), a gene which is the cell cycle-regulated component of the mitotic cyclin degradation system. Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC23. The function of CDC23 has been established by previous studies. is the cell cycle-regulated component of the mitotic cyclin degradation system.

[51587] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51588] Yu, H.; Peters, J.-M.; King, R. W.; Page, A. M.; Hieter, P.; Kirschner, M. W. : Identification of a cullin homology region in a subunit of the anaphase-promoting complex.

Science 279: 1219–1222, 1998. ; and

[51589] Zhao, N.; Lai, F.; Fernald, A. A.; Eisenbart, J. D.; Espinosa, R., III.; Wang, P. W.; Le Beau, M. M. : Human CDC23: cDNA cloning, mapping to 5q31, genomic structure, and evaluation as a.

[51590] Further studies establishing the function and utilities of CDC23 are found in John Hopkins OMIM database record ID 603462, and in cited publications numbered 2878–2879 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Egl Nine Homolog 3 (C. elegans) (EGLN3, Accession NM_022073) is another VGAM1492 host target gene. EGLN3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EGLN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN3 BINDING SITE, designated SEQ ID:22617, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51591] Another function of VGAM1492 is therefore inhibition of Egl Nine Homolog 3 (C. elegans) (EGLN3, Accession NM_022073), a gene which is an essential component of

the pathway. Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN3. The function of EGLN3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM206.Peroxisomal Farnesylated Protein (PXF, Accession NM_002857) is another VGAM1492 host target gene. PXF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXF BINDING SITE, designated SEQ ID:8749, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51592] Another function of VGAM1492 is therefore inhibition of Peroxisomal Farnesylated Protein (PXF, Accession NM_002857), a gene which may function in peroxisomal biogenesis or assembly. Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXF. The function of PXF and its association with various dis-

eases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281) is another VGAM1492 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42829, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51593] Another function of VGAM1492 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A. KIAA1260 (Accession XM_010461) is another VGAM1492 host target gene. KIAA1260 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1260, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1260 BINDING SITE, designated SEQ ID:30156, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51594] Another function of VGAM1492 is therefore inhibition of KIAA1260 (Accession XM_010461). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1260. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM1492 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12799, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51595] Another function of VGAM1492 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM1492 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with LASP1. Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540) is another VGAM1492 host target gene. NCOA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NCOA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA2 BINDING SITE, designated SEQ ID:13293, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51596] Another function of VGAM1492 is therefore inhibition of Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA2. SNRK (Accession NM_017719) is another VGAM1492 host target gene. SNRK BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of SNRK BINDING SITE, designated SEQ ID:19306, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51597] Another function of VGAM1492 is therefore inhibition of SNRK (Accession NM_017719). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNRK. LOC145662 (Accession XM_085194) is another VGAM1492 host target gene. LOC145662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145662 BINDING SITE, designated SEQ ID:37917, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51598] Another function of VGAM1492 is therefore inhibition of LOC145662 (Accession XM_085194). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145662. LOC203350 (Accession XM_117536) is another VGAM1492 host target gene. LOC203350 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43530, to the nucleotide sequence of VGAM1492 RNA, herein designated VGAM RNA, also designated SEQ ID:4203.

[51599] Another function of VGAM1492 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM1492 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1493 (VGAM1493) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51600] VGAM1493 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1493 was detected is described hereinabove with reference to Figs. 1-8.

[51601] VGAM1493 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Johnsongrass Mosaic Virus. VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51602] VGAM1493 gene encodes a VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1493 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1493 precursor RNA is designated SEQ ID:1479, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1479 is located at position 7469 relative to the genome of Johnsongrass Mosaic Virus.

[51603] VGAM1493 precursor RNA folds onto itself, forming VGAM1493 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence

of the nucleotide sequence of the second half thereof.

[51604] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1493 folded precursor RNA into VGAM1493 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM1493 RNA is designated SEQ ID:4204, and is provided hereinbelow with reference to the sequence listing part.

[51605] VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1493 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51606] VGAM1493 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1493 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1493 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1493 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51607] The complementary binding of VGAM1493 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1493 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE

II and BINDING SITE III, inhibits translation of VGAM1493 host target RNA into VGAM1493 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51608] It is appreciated that VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1493 host target genes. The mRNA of each one of this plurality of VGAM1493 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1493 RNA, herein designated VGAM RNA, and which when bound by VGAM1493 RNA causes inhibition of translation of respective one or more VGAM1493 host target proteins.

[51609] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1493 gene, herein designated VGAM GENE, on one or more VGAM1493 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51610] It is yet further appreciated that a function of VGAM1493 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of viral infection by Johnsongrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1493 correlate with, and may be deduced from, the identity of the host target genes which VGAM1493 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51611] Nucleotide sequences of the VGAM1493 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1493 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1493 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM1493 are further described hereinbelow with reference to Table 1.

[51612] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1493 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1493 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51613] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1493 gene, herein designated VGAM is inhibition of expression of VGAM1493 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1493 correlate with, and may be deduced from, the identity of the target genes which VGAM1493 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51614] LIM Domain Kinase 1 (LIMK1, Accession NM_002314) is a VGAM1493 host target gene. LIMK1 BINDING SITE1 and LIMK1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LIMK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE1 and LIMK1 BINDING SITE2, designated SEQ ID:8123 and SEQ ID:18794 respectively, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51615] A function of VGAM1493 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_002314). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Nidogen (enactin) (NID, Accession NM_002508) is another VGAM1493 host target gene. NID BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NID, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NID BINDING SITE, designated SEQ ID:8339, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51616] Another function of VGAM1493 is therefore inhibition of Nidogen (enactin) (NID, Accession NM_002508). Accordingly, utilities of VGAM1493 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with NID. PDGFA Associated Protein 1 (PDAP1, Accession XM_166484) is another VGAM1493 host target gene. PDAP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDAP1 BINDING SITE, designated SEQ ID:44421, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51617] Another function of VGAM1493 is therefore inhibition of PDGFA Associated Protein 1 (PDAP1, Accession XM_166484). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDAP1. Ribosomal Protein L17 (RPL17, Accession NM_000985) is another VGAM1493 host target gene. RPL17 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RPL17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of RPL17 BINDING SITE, designated SEQ ID:6695, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51618] Another function of VGAM1493 is therefore inhibition of Ribosomal Protein L17 (RPL17, Accession NM_000985). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPL17. TEM8 (Accession NM_032208) is another VGAM1493 host target gene. TEM8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM8 BINDING SITE, designated SEQ ID:25916, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51619] Another function of VGAM1493 is therefore inhibition of TEM8 (Accession NM_032208), a gene which is a tumor-specific endothelial marker. Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM8.

The function of TEM8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1489. Zinc Finger Protein 264 (ZNF264, Accession NM_003417) is another VGAM1493 host target gene. ZNF264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF264 BINDING SITE, designated SEQ ID:9454, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51620] Another function of VGAM1493 is therefore inhibition of Zinc Finger Protein 264 (ZNF264, Accession NM_003417). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF264. Rho Guanine Exchange Factor (GEF) 16 (ARHGEF16, Accession NM_014448) is another VGAM1493 host target gene. ARHGEF16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGEF16, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF16 BINDING SITE, designated SEQ ID:15799, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51621] Another function of VGAM1493 is therefore inhibition of Rho Guanine Exchange Factor (GEF) 16 (ARHGEF16, Accession NM_014448). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF16. DKFZp761J139 (Accession NM_032280) is another VGAM1493 host target gene. DKFZp761J139 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp761J139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761J139 BINDING SITE, designated SEQ ID:26033, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51622] Another function of VGAM1493 is therefore inhibition of DKFZp761J139 (Accession NM_032280). Accordingly, util-

ities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761J139. DKFZp761N0624 (Accession NM_032295) is another VGAM1493 host target gene. DKFZp761N0624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761N0624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761N0624 BINDING SITE, designated SEQ ID:26073, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51623] Another function of VGAM1493 is therefore inhibition of DKFZp761N0624 (Accession NM_032295). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761N0624. DKFZp762E1511 (Accession XM_003460) is another VGAM1493 host target gene. DKFZp762E1511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762E1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762E1511 BINDING SITE, designated SEQ ID:29932, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51624] Another function of VGAM1493 is therefore inhibition of DKFZp762E1511 (Accession XM_003460). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762E1511. FLJ14917 (Accession NM_032861) is another VGAM1493 host target gene. FLJ14917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14917 BINDING SITE, designated SEQ ID:26666, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51625] Another function of VGAM1493 is therefore inhibition of FLJ14917 (Accession NM_032861). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ14917. KIAA1237 (Accession XM_087386) is another VGAM1493 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ ID:39219, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51626] Another function of VGAM1493 is therefore inhibition of KIAA1237 (Accession XM_087386). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. Neuropilin (NRP) and Tolloid (TLL)-like 2 (NETO2, Accession NM_018092) is another VGAM1493 host target gene. NETO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NETO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NETO2 BINDING SITE, designated SEQ ID:19861, to the nucleotide sequence of

VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51627] Another function of VGAM1493 is therefore inhibition of Neuropilin (NRP) and Tolloid (TLL)-like 2 (NETO2, Accession NM_018092). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NETO2. Transient Receptor Potential Cation Channel, Subfamily M, Member 3 (TRPM3, Accession XM_036123) is another VGAM1493 host target gene. TRPM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM3 BINDING SITE, designated SEQ ID:32391, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51628] Another function of VGAM1493 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 3 (TRPM3, Accession XM_036123). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with TRPM3. LOC142820 (Accession XM_084353) is another VGAM1493 host target gene. LOC142820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC142820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142820 BINDING SITE, designated SEQ ID:37561, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51629] Another function of VGAM1493 is therefore inhibition of LOC142820 (Accession XM_084353). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142820. LOC163682 (Accession XM_099402) is another VGAM1493 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42088, to the nucleotide sequence of VGAM1493 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4204.

[51630] Another function of VGAM1493 is therefore inhibition of LOC163682 (Accession XM_099402). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. LOC51312 (Accession NM_018579) is another VGAM1493 host target gene. LOC51312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51312, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51312 BINDING SITE, designated SEQ ID:20658, to the nucleotide sequence of VGAM1493 RNA, herein designated VGAM RNA, also designated SEQ ID:4204.

[51631] Another function of VGAM1493 is therefore inhibition of LOC51312 (Accession NM_018579). Accordingly, utilities of VGAM1493 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51312. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1494 (VGAM1494) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51632] VGAM1494 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1494 was detected is described hereinabove with reference to Figs. 1–8.

[51633] VGAM1494 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Johnsongrass Mosaic Virus. VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51634] VGAM1494 gene encodes a VGAM1494 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1494 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1494 precursor RNA is designated SEQ ID:1480, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1480 is located at position 656 relative to the genome of Johnsongrass Mosaic Virus.

[51635] VGAM1494 precursor RNA folds onto itself, forming

VGAM1494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51636] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1494 folded precursor RNA into VGAM1494 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM1494 RNA is designated SEQ ID:4205, and is provided hereinbelow with reference to the sequence listing part.

[51637] VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1494 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51638] VGAM1494 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1494 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1494 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51639] The complementary binding of VGAM1494 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1494 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1494 host target RNA into VGAM1494 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51640] It is appreciated that VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1494 host target genes. The mRNA of each one of this plurality of VGAM1494 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1494 RNA, herein designated VGAM RNA, and which when bound by VGAM1494 RNA causes inhibition of translation of respective one or more VGAM1494 host target proteins.

[51641] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1494 gene, herein designated VGAM GENE, on one or more VGAM1494 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51642] It is yet further appreciated that a function of VGAM1494 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of viral infection by Johnsongrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1494 correlate with, and may be deduced from, the identity of the host target genes which VGAM1494 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[51643] Nucleotide sequences of the VGAM1494 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1494 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1494 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1494 are further described hereinbelow with reference to Table 1.

[51644] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1494 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1494 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51645] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1494 gene, herein designated VGAM is inhibition of expression of VGAM1494 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1494 correlate with, and may be deduced from, the identity of the target genes which VGAM1494 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[51646] Calcium Channel, Voltage-dependent, Alpha 2/delta 3 Subunit (CACNA2D3, Accession NM_018398) is a VGAM1494 host target gene. CACNA2D3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CACNA2D3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA2D3 BINDING SITE, designated SEQ ID:20434, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51647] A function of VGAM1494 is therefore inhibition of Calcium Channel, Voltage-dependent, Alpha 2/delta 3 Subunit (CACNA2D3, Accession NM_018398). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA2D3. Folate Receptor 1 (adult) (FOLR1, Accession NM_016730) is another VGAM1494 host target gene. FOLR1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FOLR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of FOLR1 BINDING SITE, designated SEQ ID:18781, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51648] Another function of VGAM1494 is therefore inhibition of Folate Receptor 1 (adult) (FOLR1, Accession NM_016730), a gene which binds and initiates transport of folate and methotrexate. Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOLR1. The function of FOLR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM399.Sp3 Transcription Factor (SP3, Accession XM_092672) is another VGAM1494 host target gene. SP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP3 BINDING SITE, designated SEQ ID:40135, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4205.

[51649] Another function of VGAM1494 is therefore inhibition of Sp3 Transcription Factor (SP3, Accession XM_092672), a gene which binds to gt and gc boxes promoters elements. Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP3. The function of SP3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM861. COP9 (Accession NM_006710) is another VGAM1494 host target gene. COP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COP9 BINDING SITE, designated SEQ ID:13533, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51650] Another function of VGAM1494 is therefore inhibition of COP9 (Accession NM_006710). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COP9.

KIAA0303 (Accession XM_045292) is another VGAM1494 host target gene. KIAA0303 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0303 BINDING SITE, designated SEQ ID:34423, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51651] Another function of VGAM1494 is therefore inhibition of KIAA0303 (Accession XM_045292). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0303. KIAA1007 (Accession XM_168026) is another VGAM1494 host target gene. KIAA1007 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1007 BINDING SITE, designated SEQ ID:44947, to the nucleotide sequence of VGAM1494 RNA, herein design-

nated VGAM RNA, also designated SEQ ID:4205.

[51652] Another function of VGAM1494 is therefore inhibition of KIAA1007 (Accession XM_168026). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1007. KIAA1336 (Accession XM_051306) is another VGAM1494 host target gene. KIAA1336 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1336 BINDING SITE, designated SEQ ID:35798, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51653] Another function of VGAM1494 is therefore inhibition of KIAA1336 (Accession XM_051306). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1336. NY-REN-60 (Accession XM_040506) is another VGAM1494 host target gene. NY-REN-60 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-60, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-60 BINDING SITE, designated SEQ ID:33318, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51654] Another function of VGAM1494 is therefore inhibition of NY-REN-60 (Accession XM_040506). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-60. LOC152190 (Accession XM_045692) is another VGAM1494 host target gene. LOC152190 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152190 BINDING SITE, designated SEQ ID:34523, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51655] Another function of VGAM1494 is therefore inhibition of LOC152190 (Accession XM_045692). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC152190. LOC257471 (Accession XM_171020) is another VGAM1494 host target gene. LOC257471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257471 BINDING SITE, designated SEQ ID:45787, to the nucleotide sequence of VGAM1494 RNA, herein designated VGAM RNA, also designated SEQ ID:4205.

[51656] Another function of VGAM1494 is therefore inhibition of LOC257471 (Accession XM_171020). Accordingly, utilities of VGAM1494 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257471. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1495 (VGAM1495) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51657] VGAM1495 is a novel bioinformatically detected regula-

tory, non protein coding, viral micro RNA (miRNA) gene.

The method by which VGAM1495 was detected is described hereinabove with reference to Figs. 1–8.

[51658] VGAM1495 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Johnsongrass Mosaic Virus. VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51659] VGAM1495 gene encodes a VGAM1495 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1495 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1495 precursor RNA is designated SEQ ID:1481, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1481 is located at position 5140 relative to the genome of Johnsongrass Mosaic Virus.

[51660] VGAM1495 precursor RNA folds onto itself, forming VGAM1495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by

miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51661] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1495 folded precursor RNA into VGAM1495 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM1495 RNA is designated SEQ ID:4206, and is provided hereinbelow with reference to the sequence listing part.

[51662] VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1495 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51663] VGAM1495 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1495 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1495 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51664] The complementary binding of VGAM1495 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM1495 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1495 host target RNA into VGAM1495 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51665] It is appreciated that VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1495 host target genes. The mRNA of each one of this plurality of VGAM1495 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1495 RNA, herein designated VGAM RNA, and which when bound by VGAM1495 RNA causes inhibition of translation of respective one or more VGAM1495 host target proteins.

[51666] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1495 gene, herein designated VGAM GENE, on one or more VGAM1495 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51667] It is yet further appreciated that a function of VGAM1495 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of viral infection by Johnsongrass Mosaic Virus. Specific functions, and accordingly utilities, of VGAM1495 correlate with, and may be deduced from, the identity of the host target genes which VGAM1495 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51668] Nucleotide sequences of the VGAM1495 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM1495 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1495 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1495 are further described hereinbelow with reference to Table 1.

[51669] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1495 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1495 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51670] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1495 gene, herein designated VGAM is inhibition of expression of VGAM1495 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1495 correlate with, and may be deduced from, the identity of the target genes which VGAM1495 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51671] G Protein-coupled Receptor Kinase 7 (GPRK7, Accession NM_139209) is a VGAM1495 host target gene. GPRK7 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by GPRK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRK7 BINDING SITE, designated SEQ ID:29229, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51672] A function of VGAM1495 is therefore inhibition of G Protein-coupled Receptor Kinase 7 (GPRK7, Accession NM_139209), a gene which may play a role in signal transduction pathways that involve calcium as a second messenger. Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRK7. The function of GPRK7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM640.CAGE (Accession XM_095071) is another VGAM1495 host target gene. CAGE BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CAGE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of CAGE BINDING SITE, designated SEQ ID:40245, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51673] Another function of VGAM1495 is therefore inhibition of CAGE (Accession XM_095071). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAGE. FLJ20079 (Accession NM_017656) is another VGAM1495 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19169, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51674] Another function of VGAM1495 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. HSA250839 (Accession NM_018401) is another

VGAM1495 host target gene. HSA250839 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA250839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA250839 BINDING SITE, designated SEQ ID:20437, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51675] Another function of VGAM1495 is therefore inhibition of HSA250839 (Accession NM_018401). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA250839. KIAA0376 (Accession XM_037759) is another VGAM1495 host target gene. KIAA0376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0376 BINDING SITE, designated SEQ ID:32672, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51676] Another function of VGAM1495 is therefore inhibition of KIAA0376 (Accession XM_037759). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0376. pcnp (Accession NM_020357) is another VGAM1495 host target gene. pcnp BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by pcnp, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of pcnp BINDING SITE, designated SEQ ID:21626, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51677] Another function of VGAM1495 is therefore inhibition of pcnp (Accession NM_020357). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with pcnp. LOC145854 (Accession XM_085259) is another VGAM1495 host target gene. LOC145854 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145854, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145854 BINDING SITE, designated SEQ ID:38006, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51678] Another function of VGAM1495 is therefore inhibition of LOC145854 (Accession XM_085259). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145854. LOC152271 (Accession XM_087419) is another VGAM1495 host target gene. LOC152271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152271 BINDING SITE, designated SEQ ID:39238, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51679] Another function of VGAM1495 is therefore inhibition of LOC152271 (Accession XM_087419). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC152271. LOC152315 (Accession XM_087440) is another VGAM1495 host target gene. LOC152315 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152315 BINDING SITE, designated SEQ ID:39256, to the nucleotide sequence of VGAM1495 RNA, herein designated VGAM RNA, also designated SEQ ID:4206.

[51680] Another function of VGAM1495 is therefore inhibition of LOC152315 (Accession XM_087440). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152315. LOC219919 (Accession XM_167785) is another VGAM1495 host target gene. LOC219919 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219919 BINDING SITE, designated SEQ ID:44799, to the nucleotide sequence of VGAM1495 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4206.

[51681] Another function of VGAM1495 is therefore inhibition of LOC219919 (Accession XM_167785). Accordingly, utilities of VGAM1495 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219919. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1496 (VGAM1496) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51682] VGAM1496 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1496 was detected is described hereinabove with reference to Figs. 1–8.

[51683] VGAM1496 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51684] VGAM1496 gene encodes a VGAM1496 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM1496 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1496 precursor RNA is designated SEQ ID:1482, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1482 is located at position 110360 relative to the genome of Alcelaphine Herpesvirus 1.

- [51685] VGAM1496 precursor RNA folds onto itself, forming VGAM1496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51686] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1496 folded precursor RNA into VGAM1496 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM1496 RNA is designated SEQ ID:4207, and is provided hereinbelow with reference to the sequence listing part.

[51687] VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1496 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51688] VGAM1496 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1496 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1496 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51689] The complementary binding of VGAM1496 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1496 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1496 host target RNA into VGAM1496 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51690] It is appreciated that VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1496 host target genes. The mRNA of

each one of this plurality of VGAM1496 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1496 RNA, herein designated VGAM RNA, and which when bound by VGAM1496 RNA causes inhibition of translation of respective one or more VGAM1496 host target proteins.

[51691] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1496 gene, herein designated VGAM GENE, on one or more VGAM1496 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[51692] It is yet further appreciated that a function of VGAM1496 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1496 correlate with, and may be deduced from, the identity of the host target genes which VGAM1496 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51693] Nucleotide sequences of the VGAM1496 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1496 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1496 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1496 are further described hereinbelow with reference to Table 1.

[51694] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1496 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1496 RNA,

herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51695] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1496 gene, herein designated VGAM is inhibition of expression of VGAM1496 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1496 correlate with, and may be deduced from, the identity of the target genes which VGAM1496 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51696] Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487) is a VGAM1496 host target gene. CDKN2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2B BINDING SITE, designated SEQ ID:27807, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51697] A function of VGAM1496 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4)

(CDKN2B, Accession NM_078487). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2B. ATIP1 (Accession NM_020749) is another VGAM1496 host target gene. ATIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATIP1 BINDING SITE, designated SEQ ID:21860, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51698] Another function of VGAM1496 is therefore inhibition of ATIP1 (Accession NM_020749). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATIP1. DKFZp761D221 (Accession NM_032291) is another VGAM1496 host target gene. DKFZp761D221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZp761D221 BINDING SITE, designated SEQ ID:26054, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51699] Another function of VGAM1496 is therefore inhibition of DKFZp761D221 (Accession NM_032291). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D221. FLJ00026 (Accession XM_036307) is another VGAM1496 host target gene. FLJ00026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00026 BINDING SITE, designated SEQ ID:32425, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51700] Another function of VGAM1496 is therefore inhibition of FLJ00026 (Accession XM_036307). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

FLJ00026. HCA127 (Accession NM_018684) is another VGAM1496 host target gene. HCA127 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HCA127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA127 BINDING SITE, designated SEQ ID:20755, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51701] Another function of VGAM1496 is therefore inhibition of HCA127 (Accession NM_018684). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCA127. Tumor Protein D52 (TPD52, Accession NM_005079) is another VGAM1496 host target gene. TPD52 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TPD52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPD52 BINDING SITE, designated SEQ ID:11529, to the nucleotide sequence of VGAM1496 RNA,

herein designated VGAM RNA, also designated SEQ ID:4207.

[51702] Another function of VGAM1496 is therefore inhibition of Tumor Protein D52 (TPD52, Accession NM_005079). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPD52. LOC115073 (Accession XM_055193) is another VGAM1496 host target gene. LOC115073 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115073 BINDING SITE, designated SEQ ID:36235, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51703] Another function of VGAM1496 is therefore inhibition of LOC115073 (Accession XM_055193). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115073. LOC221641 (Accession XM_168090) is another VGAM1496 host target gene. LOC221641 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221641 BINDING SITE, designated SEQ ID:45007, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51704] Another function of VGAM1496 is therefore inhibition of LOC221641 (Accession XM_168090). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221641. LOC91250 (Accession XM_037135) is another VGAM1496 host target gene. LOC91250 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91250, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91250 BINDING SITE, designated SEQ ID:32545, to the nucleotide sequence of VGAM1496 RNA, herein designated VGAM RNA, also designated SEQ ID:4207.

[51705] Another function of VGAM1496 is therefore inhibition of

LOC91250 (Accession XM_037135). Accordingly, utilities of VGAM1496 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91250. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1497 (VGAM1497) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51706] VGAM1497 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1497 was detected is described hereinabove with reference to Figs. 1-8.

[51707] VGAM1497 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51708] VGAM1497 gene encodes a VGAM1497 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1497 precursor RNA does not encode a protein. A

nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1497 precursor RNA is designated SEQ ID:1483, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1483 is located at position 108884 relative to the genome of Alcelaphine Herpesvirus 1.

- [51709] VGAM1497 precursor RNA folds onto itself, forming VGAM1497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51710] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1497 folded precursor RNA into VGAM1497 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM1497 RNA is designated SEQ ID:4208, and is provided hereinbelow with reference to the sequence listing part.

[51711] VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1497 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51712] VGAM1497 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1497 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM1497 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[51713] The complementary binding of VGAM1497 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1497 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1497 host target RNA into VGAM1497 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51714] It is appreciated that VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1497 host target genes. The mRNA of each one of this plurality of VGAM1497 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM1497 RNA, herein designated VGAM RNA, and which when bound by VGAM1497 RNA causes inhibition of translation of respective one or more VGAM1497 host target proteins.

[51715] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1497 gene, herein designated VGAM GENE, on one or more VGAM1497 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51716] It is yet further appreciated that a function of VGAM1497

is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1497 correlate with, and may be deduced from, the identity of the host target genes which VGAM1497 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51717] Nucleotide sequences of the VGAM1497 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1497 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1497 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1497 are further described hereinbelow with reference to Table 1.

[51718] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1497 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1497 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51719] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1497 gene, herein designated VGAM is inhibition of expression of VGAM1497 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1497 correlate with, and may be deduced from, the identity of the target genes which VGAM1497 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51720] B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707) is a VGAM1497 host target gene. BCL7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7B BINDING SITE, designated SEQ ID:7434, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51721] A function of VGAM1497 is therefore inhibition of B-cell CLL/lymphoma 7B (BCL7B, Accession NM_001707), a gene which is of yet unknown function. Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL7B.

The function of BCL7B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1189. Transcription Factor 12 (HTF4, helix-loop-helix transcription factors 4) (TCF12, Accession NM_003205) is another VGAM1497 host target gene. TCF12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF12 BINDING SITE, designated SEQ ID:9200, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51722] Another function of VGAM1497 is therefore inhibition of Transcription Factor 12 (HTF4, helix-loop-helix transcription factors 4) (TCF12, Accession NM_003205), a gene which may play important roles during development of the nervous system as well as in other organ systems. Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF12. The function of TCF12 and its association with various diseases and clinical conditions, has

been established by previous studies, as described herein above with reference to VGAM308.DKFZP564O043 (Accession XM_166502) is another VGAM1497 host target gene. DKFZP564O043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O043 BINDING SITE, designated SEQ ID:44429, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51723] Another function of VGAM1497 is therefore inhibition of DKFZP564O043 (Accession XM_166502). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O043. HYA22 (Accession NM_005808) is another VGAM1497 host target gene. HYA22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HYA22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYA22 BIND-

ING SITE, designated SEQ ID:12386, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51724] Another function of VGAM1497 is therefore inhibition of HYA22 (Accession NM_005808). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYA22. KIAA0652 (Accession NM_014741) is another VGAM1497 host target gene. KIAA0652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0652 BINDING SITE, designated SEQ ID:16407, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51725] Another function of VGAM1497 is therefore inhibition of KIAA0652 (Accession NM_014741). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0652. KIAA0836 (Accession XM_035390) is another VGAM1497 host target gene. KIAA0836 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0836 BINDING SITE, designated SEQ ID:32245, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51726] Another function of VGAM1497 is therefore inhibition of KIAA0836 (Accession XM_035390). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. RCD-8 (Accession NM_014329) is another VGAM1497 host target gene. RCD-8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RCD-8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RCD-8 BINDING SITE, designated SEQ ID:15642, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51727] Another function of VGAM1497 is therefore inhibition of

RCD-8 (Accession NM_014329). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RCD-8. Syntaxin 3A (STX3A, Accession NM_004177) is another VGAM1497 host target gene. STX3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STX3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STX3A BINDING SITE, designated SEQ ID:10389, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51728] Another function of VGAM1497 is therefore inhibition of Syntaxin 3A (STX3A, Accession NM_004177). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STX3A. LOC149134 (Accession XM_097594) is another VGAM1497 host target gene. LOC149134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC149134 BINDING SITE, designated SEQ ID:40958, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51729] Another function of VGAM1497 is therefore inhibition of LOC149134 (Accession XM_097594). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149134. LOC197335 (Accession XM_113866) is another VGAM1497 host target gene. LOC197335 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197335 BINDING SITE, designated SEQ ID:42480, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51730] Another function of VGAM1497 is therefore inhibition of LOC197335 (Accession XM_113866). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197335. LOC220522 (Accession XM_018306) is an-

other VGAM1497 host target gene. LOC220522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220522 BINDING SITE, designated SEQ ID:30352, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51731] Another function of VGAM1497 is therefore inhibition of LOC220522 (Accession XM_018306). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220522. LOC92573 (Accession XM_045884) is another VGAM1497 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34593, to the nucleotide sequence of VGAM1497 RNA, herein designated VGAM RNA, also designated SEQ ID:4208.

[51732] Another function of VGAM1497 is therefore inhibition of LOC92573 (Accession XM_045884). Accordingly, utilities of VGAM1497 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92573. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1498 (VGAM1498) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51733] VGAM1498 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1498 was detected is described hereinabove with reference to Figs. 1–8.

[51734] VGAM1498 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51735] VGAM1498 gene encodes a VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes,

VGAM1498 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1498 precursor RNA is designated SEQ ID:1484, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1484 is located at position 112274 relative to the genome of Alcelaphine Herpesvirus 1.

[51736] VGAM1498 precursor RNA folds onto itself, forming VGAM1498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51737] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1498 folded precursor RNA into VGAM1498 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 52%) nucleotide sequence of VGAM1498 RNA is designated SEQ ID:4209, and is provided hereinbelow with reference to the sequence listing part.

[51738] VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1498 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[51739] VGAM1498 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1498 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1498 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51740] The complementary binding of VGAM1498 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1498 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1498 host target RNA into VGAM1498 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51741] It is appreciated that VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1498 host target genes. The mRNA of each one of this plurality of VGAM1498 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1498 RNA, herein designated VGAM RNA, and which when bound by VGAM1498 RNA causes inhibition of translation of respective one or more VGAM1498 host target proteins.

[51742] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1498 gene, herein designated VGAM GENE, on one or more VGAM1498 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51743] It is yet further appreciated that a function of VGAM1498 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1498 correlate with, and may be deduced from, the identity of the host target genes which VGAM1498 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51744] Nucleotide sequences of the VGAM1498 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1498 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1498 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1498 are further described hereinbelow with reference to Table 1.

[51745] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1498 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1498 RNA, herein designated VGAM RNA, are described hereinbelow

with reference to Table 2.

[51746] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1498 gene, herein designated VGAM is inhibition of expression of VGAM1498 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1498 correlate with, and may be deduced from, the identity of the target genes which VGAM1498 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51747] CARP (Accession NM_014391) is a VGAM1498 host target gene. CARP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CARP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CARP BINDING SITE, designated SEQ ID:15720, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51748] A function of VGAM1498 is therefore inhibition of CARP (Accession NM_014391). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CARP. CGTHBA (Accession NM_012075) is another VGAM1498

host target gene. CGTHBA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CGTHBA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGTHBA BINDING SITE, designated SEQ ID:14359, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51749] Another function of VGAM1498 is therefore inhibition of CGTHBA (Accession NM_012075). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGTHBA. Calponin 2 (CNN2, Accession NM_004368) is another VGAM1498 host target gene. CNN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNN2 BINDING SITE, designated SEQ ID:10584, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51750] Another function of VGAM1498 is therefore inhibition of Calponin 2 (CNN2, Accession NM_004368), a gene which may be involved in the structural organization and/or anchorage of actin filaments. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNN2. The function of CNN2 has been established by previous studies. Masuda et al. (1996) cloned a cDNA encoding calponin-2 (CNN2) by screening a human heart cDNA library with a CNN1 (OMIM Ref. No. 600806) cDNA. The CNN2 protein is 94.8% identical to mouse calponin h2 (see OMIM Ref. No. 600806), indicating that these proteins are homologs. The predicted CNN2 protein has 309 amino acids and a pI of 7.1. It contains motifs that are present in CNN1 and CNN3 (OMIM Ref. No. 602374): 3 tandem repeats of 29 amino acids, an actin-binding domain, a VAV (OMIM Ref. No. 164875)-homologous region, and 2 consensus phosphorylation sites for tyrosine kinase at the C terminus. The 3-prime untranslated region of the CNN2 mRNA contains an Alu repetitive sequence in the anti-sense direction. RT-PCR detected CNN2 transcripts in both cultured smooth muscle and nonmuscle cells and showed that mouse calponin h2 is expressed in embryonic

and adult heart. CNN2 protein localizes to the cell-to-cell junctions of cardiomyocytes and codistributes with vinculin (OMIM Ref. No. 193065). Masuda et al. (1996) suggested that CNN2 may be involved in the structural organization and/or anchorage of actin filaments and may function in the cell adhesion mechanism Cheng et al. (1994) mapped the CNN2 gene to 21q11.1 by hybridization to chromosome 21q-specific YACs.

[51751] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51752] Masuda, H.; Tanaka, K.; Takagi, M.; Ohgami, K.; Sakamaki, T.; Shibata, N.; Takahashi, K. : Molecular cloning and characterization of human non-smooth muscle calponin. J. Biochem. 120: 415-424, 1996. ; and

[51753] Cheng, J.-F.; Boyartchuk, V.; Zhu, Y. : Isolation and mapping of human chromosome 21 cDNA: progress in constructing a chromosome 21 expression map. Genomics 23: 75-84, 1994.

[51754] Further studies establishing the function and utilities of CNN2 are found in John Hopkins OMIM database record ID 602373, and in cited publications numbered 8674 listed in the bibliography section hereinbelow, which are also

hereby incorporated by reference. Collagen, Type XV, Alpha 1 (COL15A1, Accession NM_001855) is another VGAM1498 host target gene. COL15A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL15A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL15A1 BINDING SITE, designated SEQ ID:7589, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51755] Another function of VGAM1498 is therefore inhibition of Collagen, Type XV, Alpha 1 (COL15A1, Accession NM_001855), a gene which may be involved in maintaining the structure of connective tissue. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL15A1. The function of COL15A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM304. Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455) is another VGAM1498 host target gene. EXTL1 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by EXTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL1 BINDING SITE, designated SEQ ID:10755, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51756] Another function of VGAM1498 is therefore inhibition of Exostoses (multiple)-like 1 (EXTL1, Accession NM_004455), a gene which probably contribute to the synthesis of heparan sulfate and heparin. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL1. The function of EXTL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM806.Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293) is another VGAM1498 host target gene. LAMC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LAMC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMC1 BINDING SITE, designated SEQ ID:8073, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51757] Another function of VGAM1498 is therefore inhibition of Laminin, Gamma 1 (formerly LAMB2) (LAMC1, Accession NM_002293), a gene which may mediate the attachment, migration, and organization of cells into tissues. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMC1. The function of LAMC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM812.2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM_002535) is another VGAM1498 host target gene. OAS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS2 BINDING SITE, designated SEQ ID:8373, to the nucleotide se-

quence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51758] Another function of VGAM1498 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 2, 69/71kDa (OAS2, Accession NM_002535), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS2. The function of OAS2 has been established by previous studies. The 2-prime,5-prime oligoadenylate synthetases (OASs) are interferon-induced proteins characterized by their capacity to catalyze the synthesis of 2-prime,5-prime oligomers of adenosine (2-5As). See OAS1 (OMIM Ref. No. 164350). Hovanessian et al. (1987) found that interferon-treated human cells contain several OASs corresponding to proteins of 40 (OAS1), 46 (OAS1), 69, and 100 (OMIM Ref. No. 603351) kD. Marie et al. (1989) generated highly specific polyclonal antibodies against p69, the 69-kD OAS. By screening an interferon-treated human cell expression library with the anti-p69 antibodies, Marie and Hovanessian (1992) isolated a partial OAS2 cDNA. They screened additional libraries with

the partial cDNA and recovered cDNAs encoding 2 OAS2 isoforms. The smaller isoform is encoded by 2 mRNAs that differ in the length of the 3-prime untranslated region. Northern blot analysis revealed that OAS2 is expressed as 4 interferon-induced mRNAs in human cells. The predicted OAS2 proteins have a common 683-amino acid sequence and different 3-prime termini. By SDS-PAGE of in vitro transcription/translation products, the authors showed that 2 isoforms have molecular masses of 69 and 71 kD. Both isoforms exhibited OAS activity in vitro. Sequence analysis indicated that OAS2 contains 2 OAS1-homologous domains separated by a proline-rich putative linker region. The N- and C-terminal domains are 41% and 53% identical to OAS1, respectively. Marie and Hovanessian (1992) suggested that the OAS2 gene derived from the fusion of 2 ancestral genes analogous to OAS1. By fluorescence in situ hybridization and by inclusion within mapped clones, Hovnanian et al. (1998) determined that the OAS1, OAS2, and OAS3 genes are clustered with a 130-kb region on 12q24.2.

[51759] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51760] Hovnanian, A.; Rebouillat, D.; Mattei, M.-G.; Levy, E. R.; Marie, I.; Monaco, A. P.; Hovanessian, A. G. : The human 2-prime,5-prime-oligoadenylate synthetase locus is composed of three distinct genes clustered on chromosome 12q24.2 encoding the 100-, 69-, and 40-kDa forms. *Genomics* 52: 267-277, 1998. ; and

[51761] Marie, I.; Hovanessian, A. G. : The 69-kDa 2-5A synthetase is composed of two homologous and adjacent functional domains. *J. Biol. Chem.* 267: 9933-9939, 1992.

[51762] Further studies establishing the function and utilities of OAS2 are found in John Hopkins OMIM database record ID 603350, and in cited publications numbered 800 and 8010-8011 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM_004571) is another VGAM1498 host target gene. PKNOX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKNOX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKNOX1 BINDING SITE, designated SEQ ID:10912, to the nucleotide sequence of VGAM1498 RNA,

herein designated VGAM RNA, also designated SEQ ID:4209.

[51763] Another function of VGAM1498 is therefore inhibition of PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM_004571), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKNOX1. The function of PKNOX1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM276. Proteasome (prosome, macropain) Activator Subunit 3 (PA28 gamma; Ki) (PSME3, Accession NM_005789) is another VGAM1498 host target gene. PSME3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSME3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSME3 BINDING SITE, designated SEQ ID:12370, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51764] Another function of VGAM1498 is therefore inhibition of Proteasome (prosome, macropain) Activator Subunit 3 (PA28 gamma; Ki) (PSME3, Accession NM_005789), a gene which is the activator subunit of the proteasome (prosome macropain). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSME3. The function of PSME3 has been established by previous studies. Patients with systemic lupus erythematosus (SLE; 152700) produce autoantibodies against a number of nuclear antigens, including SNRP70 (OMIM Ref. No. 180740), PCNA (OMIM Ref. No. 176740), CDR1 (OMIM Ref. No. 302650), and Ki. By screening a human placenta cDNA library with a probe obtained by screening a bovine retina cDNA library with anti-Ki sera from an SLE patient, Nikaido et al. (1990) isolated a cDNA encoding PSME3, which they called Ki. Sequence analysis predicted that the 254-amino acid, hydrophilic PSME3 protein contains a nuclear localization signal and has a molecular mass of approximately 30 kD, close to the 32 kD observed by Western blot analysis. PSME3 shares over 99% amino acid identity with the bovine sequence. RNA blot analysis of human placenta, bovine brain, and mouse embryos detected 3.0- and

1.5-kb PSME3 transcripts. By analysis of overlapping YAC contigs and by FISH, Albertsen et al. (1994) mapped the PSME3 gene to 17q12-q21. Kandil et al. (1997) mapped the mouse Psme3 gene to chromosome 14 using inter-specific backcross analysis.

[51765] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51766] Nikaido, T.; Shimada, K.; Shibata, M.; Hata, M.; Sakamoto, M.; Takasaki, Y.; Sato, C.; Takahashi, T.; Nishida, Y. : Cloning and nucleotide sequence of cDNA for Ki antigen, a highly conserved nuclear protein detected with sera from patients with systemic lupus erythematosus. Clin. Exp. Immun. 79: 209-214, 1990. ; and

[51767] Albertsen, H. M.; Smith, S. A.; Mazoyer, S.; Fujimoto, E.; Stevens, J.; Williams, B.; Rodriguez, P.; Cropp, C. S.; Slijepcevic, P.; Carlson, M.; Robertson, M.; Bradley, P.; Lawrence, E.;

[51768] Further studies establishing the function and utilities of PSME3 are found in John Hopkins OMIM database record ID 605129, and in cited publications numbered 12201-7083 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence.Solute Carrier Family 31 (copper transporters), Member 1 (SLC31A1, Accession NM_001859) is another VGAM1498 host target gene. SLC31A1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC31A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC31A1 BINDING SITE, designated SEQ ID:7601, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51769] Another function of VGAM1498 is therefore inhibition of Solute Carrier Family 31 (copper transporters), Member 1 (SLC31A1, Accession NM_001859), a gene which is involved in high-affinity copper uptake. Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC31A1. The function of SLC31A1 has been established by previous studies. Moller et al. (2000) found that cells expressing CTR1 but not those expressing CTR2 showed a dramatic hyperaccumulation of radioactive copper, comparable to that seen in fibroblasts from Menkes disease patients. However, in contrast to the Menkes syn-

drome fibroblasts, the CTR1-expressing fibroblasts had an efflux rate similar to normal fibroblasts. Animal model experiments lend further support to the function of SLC31A1. To test the hypothesis that CTR1 is required for copper delivery to mammalian cells, Kuo et al. (2001) inactivated the Ctr1 gene in mice by targeted mutagenesis. They observed early embryonic lethality in homozygous mutant embryos and a deficiency in copper uptake in the brains of heterozygous animals. A study of the spatial and temporal expression pattern of Ctr1 during mouse development and adulthood further showed that Ctr1 is ubiquitously transcribed with highest expression observed in the specialized epithelia of the choroid plexus and renal tubules and in connective tissues of the eye, ovary, and testis. Similarly, Lee et al. (2001) showed that the mouse Ctr1 gene encodes a component of the copper transport machinery and that mice heterozygous for Ctr1 exhibit tissue-specific defects in copper accumulation and in the activities of copper-dependent enzymes. Mice completely deficient for Ctr1 exhibited profound growth and developmental defects and died in utero in midgestation

[51770] It is appreciated that the abovementioned animal model for SLC31A1 is acknowledged by those skilled in the art as

a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[51771] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51772] Lee, J.; Prohaska, J. R.; Thiele, D. J. : Essential role for mammalian copper transporter Ctr1 in copper homeostasis and embryonic development. Proc. Nat. Acad. Sci. 98: 6842–6847, 2001. ; and

[51773] Moller, L. B.; Petersen, C.; Lund, C.; Horn, N. : Characterization of the hCTR1 gene: genomic organization, functional expression, and identification of a highly homologous processed gen.

[51774] Further studies establishing the function and utilities of SLC31A1 are found in John Hopkins OMIM database record ID 603085, and in sited publications numbered 1071–1077 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. C16orf5 (Accession NM_013399) is another VGAM1498 host target gene. C16orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C16orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of C16orf5 BINDING SITE, designated SEQ ID:15054, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51775] Another function of VGAM1498 is therefore inhibition of C16orf5 (Accession NM_013399). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C16orf5. DKFZP586G1122 (Accession XM_028643) is another VGAM1498 host target gene. DKFZP586G1122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586G1122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586G1122 BINDING SITE, designated SEQ ID:30725, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51776] Another function of VGAM1498 is therefore inhibition of DKFZP586G1122 (Accession XM_028643). Accordingly, utilities of VGAM1498 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZP586G1122. Dihydropyrimidinase-like 4 (DPYSL4, Accession NM_006426) is another VGAM1498 host target gene. DPYSL4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DPYSL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL4 BINDING SITE, designated SEQ ID:13142, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51777] Another function of VGAM1498 is therefore inhibition of Dihydropyrimidinase-like 4 (DPYSL4, Accession NM_006426). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL4. FLJ13848 (Accession NM_024771) is another VGAM1498 host target gene. FLJ13848 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of FLJ13848 BINDING SITE, designated SEQ ID:24134, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51778] Another function of VGAM1498 is therefore inhibition of FLJ13848 (Accession NM_024771). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13848. FLJ14775 (Accession NM_032837) is another VGAM1498 host target gene. FLJ14775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14775 BINDING SITE, designated SEQ ID:26617, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51779] Another function of VGAM1498 is therefore inhibition of FLJ14775 (Accession NM_032837). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14775. FLJ20254 (Accession NM_017727) is another

VGAM1498 host target gene. FLJ20254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20254 BINDING SITE, designated SEQ ID:19316, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51780] Another function of VGAM1498 is therefore inhibition of FLJ20254 (Accession NM_017727). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20254. FLJ32752 (Accession NM_144666) is another VGAM1498 host target gene. FLJ32752 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ32752, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32752 BINDING SITE, designated SEQ ID:29483, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51781] Another function of VGAM1498 is therefore inhibition of FLJ32752 (Accession NM_144666). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32752. KIAA0738 (Accession NM_014719) is another VGAM1498 host target gene. KIAA0738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0738 BINDING SITE, designated SEQ ID:16276, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51782] Another function of VGAM1498 is therefore inhibition of KIAA0738 (Accession NM_014719). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0738. KIAA0953 (Accession XM_039733) is another VGAM1498 host target gene. KIAA0953 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0953, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0953 BINDING SITE, designated SEQ ID:33169, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51783] Another function of VGAM1498 is therefore inhibition of KIAA0953 (Accession XM_039733). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0953. KIAA1867 (Accession XM_170675) is another VGAM1498 host target gene. KIAA1867 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1867 BINDING SITE, designated SEQ ID:45452, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51784] Another function of VGAM1498 is therefore inhibition of KIAA1867 (Accession XM_170675). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1867. Karyopherin (importin) Beta 3 (KPNB3, Accession NM_002271) is another VGAM1498 host target gene. KPNB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KPNB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KPNB3 BINDING SITE, designated SEQ ID:8063, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51785] Another function of VGAM1498 is therefore inhibition of Karyopherin (importin) Beta 3 (KPNB3, Accession NM_002271). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KPNB3. Praja 1 (PJA1, Accession NM_022368) is another VGAM1498 host target gene. PJA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PJA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PJA1 BINDING SITE, designated SEQ ID:22756, to the nucleotide sequence of VGAM1498 RNA, herein

designated VGAM RNA, also designated SEQ ID:4209.

[51786] Another function of VGAM1498 is therefore inhibition of Praja 1 (PJA1, Accession NM_022368). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PJA1. RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM_013401) is another VGAM1498 host target gene. RAB3IL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3IL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3IL1 BINDING SITE, designated SEQ ID:15060, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51787] Another function of VGAM1498 is therefore inhibition of RAB3A Interacting Protein (rabin3)-like 1 (RAB3IL1, Accession NM_013401). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3IL1. SEC61A1 (Accession NM_013336) is another VGAM1498 host target gene. SEC61A1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by SEC61A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC61A1 BINDING SITE, designated SEQ ID:14982, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51788] Another function of VGAM1498 is therefore inhibition of SEC61A1 (Accession NM_013336). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC61A1. SKIP (Accession NM_016532) is another VGAM1498 host target gene. SKIP BINDING SITE1 and SKIP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SKIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIP BINDING SITE1 and SKIP BINDING SITE2, designated SEQ ID:18599 and SEQ ID:28262 respectively, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51789] Another function of VGAM1498 is therefore inhibition of SKIP (Accession NM_016532). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIP. LOC146890 (Accession XM_097128) is another VGAM1498 host target gene. LOC146890 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146890, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146890 BINDING SITE, designated SEQ ID:40765, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51790] Another function of VGAM1498 is therefore inhibition of LOC146890 (Accession XM_097128). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146890. LOC148758 (Accession XM_086301) is another VGAM1498 host target gene. LOC148758 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC148758, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148758 BINDING SITE, designated SEQ ID:38586, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51791] Another function of VGAM1498 is therefore inhibition of LOC148758 (Accession XM_086301). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148758. LOC149113 (Accession XM_086425) is another VGAM1498 host target gene. LOC149113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149113 BINDING SITE, designated SEQ ID:38640, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51792] Another function of VGAM1498 is therefore inhibition of LOC149113 (Accession XM_086425). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC149113. LOC154403 (Accession XM_087919) is another VGAM1498 host target gene. LOC154403 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154403, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154403 BINDING SITE, designated SEQ ID:39468, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51793] Another function of VGAM1498 is therefore inhibition of LOC154403 (Accession XM_087919). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154403. LOC154992 (Accession XM_088106) is another VGAM1498 host target gene. LOC154992 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154992 BINDING SITE, designated SEQ ID:39518, to the nucleotide sequence of VGAM1498 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:4209.

[51794] Another function of VGAM1498 is therefore inhibition of LOC154992 (Accession XM_088106). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154992. LOC201868 (Accession XM_114393) is another VGAM1498 host target gene. LOC201868 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201868, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201868 BINDING SITE, designated SEQ ID:42921, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51795] Another function of VGAM1498 is therefore inhibition of LOC201868 (Accession XM_114393). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201868. LOC222068 (Accession XM_166556) is another VGAM1498 host target gene. LOC222068 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222068, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222068 BINDING SITE, designated SEQ ID:44537, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51796] Another function of VGAM1498 is therefore inhibition of LOC222068 (Accession XM_166556). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222068. LOC93052 (Accession XM_048905) is another VGAM1498 host target gene. LOC93052 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93052 BINDING SITE, designated SEQ ID:35300, to the nucleotide sequence of VGAM1498 RNA, herein designated VGAM RNA, also designated SEQ ID:4209.

[51797] Another function of VGAM1498 is therefore inhibition of LOC93052 (Accession XM_048905). Accordingly, utilities of VGAM1498 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with LOC93052. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1499 (VGAM1499) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51798] VGAM1499 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1499 was detected is described hereinabove with reference to Figs. 1–8.

[51799] VGAM1499 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Alcelaphine Herpesvirus 1. VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51800] VGAM1499 gene encodes a VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1499 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1499 precursor RNA is desig-

nated SEQ ID:1485, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1485 is located at position 110926 relative to the genome of Alcelaphine Herpesvirus 1.

- [51801] VGAM1499 precursor RNA folds onto itself, forming VGAM1499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.
- [51802] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1499 folded precursor RNA into VGAM1499 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM1499 RNA is designated SEQ ID:4210, and is provided hereinbelow with reference to the sequence

listing part.

[51803] VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1499 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51804] VGAM1499 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1499 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1499 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51805] The complementary binding of VGAM1499 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1499 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1499 host target RNA into VGAM1499 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51806] It is appreciated that VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1499 host target genes. The mRNA of each one of this plurality of VGAM1499 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1499 RNA, herein designated VGAM

RNA, and which when bound by VGAM1499 RNA causes inhibition of translation of respective one or more VGAM1499 host target proteins.

[51807] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1499 gene, herein designated VGAM GENE, on one or more VGAM1499 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51808] It is yet further appreciated that a function of VGAM1499 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM1499 include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM1499 correlate with, and may be deduced from, the identity of the host target genes which VGAM1499 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51809] Nucleotide sequences of the VGAM1499 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1499 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1499 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1499 are further described hereinbelow with reference to Table 1.

[51810] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1499 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1499 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51811] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1499 gene, herein designated VGAM is

inhibition of expression of VGAM1499 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1499 correlate with, and may be deduced from, the identity of the target genes which VGAM1499 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51812] Cyclin-dependent Kinase Inhibitor 1B (p27, Kip1) (CDKN1B, Accession NM_004064) is a VGAM1499 host target gene. CDKN1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDKN1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN1B BINDING SITE, designated SEQ ID:10272, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51813] A function of VGAM1499 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 1B (p27, Kip1) (CDKN1B, Accession NM_004064), a gene which is involved in g1 arrest and may mediate tgf beta-induced g1 arrest. Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CDKN1B. The function of CDKN1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM592. Empty Spiracles Homolog 2 (Drosophila) (EMX2, Accession XM_113640) is another VGAM1499 host target gene. EMX2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMX2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMX2 BINDING SITE, designated SEQ ID:42314, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51814] Another function of VGAM1499 is therefore inhibition of Empty Spiracles Homolog 2 (Drosophila) (EMX2, Accession XM_113640), a gene which may function in combinations with otx1/2 to specify cell fates in the developing central nervous system. Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMX2. The function of EMX2 and its association with various diseases and clinical conditions, has been established by previous studies, as

described hereinabove with reference to VGAM510. Lysosomal-associated Membrane Protein 2 (LAMP2, Accession NM_013995) is another VGAM1499 host target gene. LAMP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LAMP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMP2 BINDING SITE, designated SEQ ID:15183, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51815] Another function of VGAM1499 is therefore inhibition of Lysosomal-associated Membrane Protein 2 (LAMP2, Accession NM_013995). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMP2. Paired Box Gene 6 (aniridia, keratitis) (PAX6, Accession NM_000280) is another VGAM1499 host target gene. PAX6 BINDING SITE1 and PAX6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PAX6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PAX6 BINDING SITE1 and PAX6 BINDING SITE2, designated SEQ ID:5825 and SEQ ID:7309 respectively, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51816] Another function of VGAM1499 is therefore inhibition of Paired Box Gene 6 (aniridia, keratitis) (PAX6, Accession NM_000280), a gene which involves in oculogenesis. Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX6. The function of PAX6 has been established by previous studies. PAX6 is a member of the paired box gene family and encodes a transcriptional regulator involved in oculogenesis, pancreatic, pituitary and central nervous system development. Hanson and Van Heyningen (1995) reviewed the work on PAX6 in man, mouse, and *Drosophila*. A chronology was provided, beginning with identification of the 'paired' gene as a key regulator of segmentation in *Drosophila* in 1980 to the discovery by Halder et al. (1995) that ectopic expression of *Drosophila* Pax6 induces ectopic eye development. Wawersik and Maas (2000) reviewed the role of Pax6 and other genes in vertebrate and fly oculogenesis. Animal

model experiments lend further support to the function of PAX6. Lyon (1988) suggested that 'small eye' (Sey) in the mouse, which is on chromosome 2, may be homologous to aniridia type II (OMIM Ref. No. 106210) inasmuch as there is a region of conserved homology of synteny between human 11p and mouse chromosome 2. This suggestion was corroborated by van der Meer-de Jong et al. (1990) who found through interspecies backcrosses for linkage mapping that the Sey gene lies between Fshb and Cas-1. In the human, AN2 lies between the 2 cognate genes, FSHB and CAT. Glaser et al. (1990) studied the Sey mutation by localizing in an interspecies backcross between *Mus musculus*/domesticus and *Mus spretus*, the region on mouse chromosome 2 carrying 9 evolutionarily conserved DNA clones from proximal human 11p. In Dickie's small eye, they found deletion of 3 clones that encompass the aniridia (AN2) and Wilms tumor susceptibility genes in man. Unlike their human counterparts, the heterozygous Dickie's small eye mice do not develop nephroblastomas. The homology of Sey and AN2 was established by the cloning of the AN2 gene in the human and its homolog in the mouse, and the demonstration of mutations in 3 independent Sey alleles (Hill et al., 1991).

The mutations would predictably disrupt the function of the gene, which belongs to the Pax multigene family. This family of developmental genes was first described in *Drosophila*. A Pax gene referred to as Pax6 is identical to the mouse homolog of the candidate aniridia gene. Matsuo et al. (1993) found an internal deletion of about 600 bp in the Pax6 gene in rats homozygous for the small eye mutation. Deletion was due to a single base insertion that generated an abnormal 5-prime donor splice site. They showed that anterior midbrain crest cells in the homozygous embryos reached the eye rudiments but did not migrate any further to the nasal rudiments, suggesting that the Pax6 gene is involved in conducting migration of neural crest cells from the anterior midbrain.

[51817] It is appreciated that the abovementioned animal model for PAX6 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[51818] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[51819] Wawersik, S.; Maas, R. L. : Vertebrate eye development as modeled in *Drosophila*. *Hum. Molec. Genet.* 9: 917–925,

2000. ; and

[51820] Glaser, T.; Lane, J.; Housman, D. : A mouse model of the aniridia–Wilms tumor deletion syndrome. Science 250: 823–827, 1990.

[51821] Further studies establishing the function and utilities of PAX6 are found in John Hopkins OMIM database record ID 607108, and in cited publications numbered 5548, 12160, 8112, 12161, 12310–12313, 5586–5588, 11658–5590, 12314, 12315, 12316–12317, 5593–5595, 12318, 12319–12320, 6139, 12162, 12321–12323, 5575, 12324, 12325–5497, 10763, 12326, 12329, 12327–550 and 1 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Down Syndrome Critical Region Gene 1–like 1 (DSCR1L1, Accession NM_005822) is another VGAM1499 host target gene. DSCR1L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DSCR1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR1L1 BINDING SITE, designated SEQ ID:12427, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also des–

ignated SEQ ID:4210.

[51822] Another function of VGAM1499 is therefore inhibition of Down Syndrome Critical Region Gene 1-like 1 (DSCR1L1, Accession NM_005822). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR1L1. FLJ14906 (Accession NM_032859) is another VGAM1499 host target gene. FLJ14906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14906 BINDING SITE, designated SEQ ID:26663, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51823] Another function of VGAM1499 is therefore inhibition of FLJ14906 (Accession NM_032859). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14906. FLJ22794 (Accession XM_166220) is another VGAM1499 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44029, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51824] Another function of VGAM1499 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. KIAA0471 (Accession NM_014857) is another VGAM1499 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16911, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51825] Another function of VGAM1499 is therefore inhibition of KIAA0471 (Accession NM_014857). Accordingly, utilities

of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. KIAA1456 (Accession XM_040100) is another VGAM1499 host target gene. KIAA1456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1456 BINDING SITE, designated SEQ ID:33263, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51826] Another function of VGAM1499 is therefore inhibition of KIAA1456 (Accession XM_040100). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1456. PRO1768 (Accession NM_014099) is another VGAM1499 host target gene. PRO1768 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1768, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1768

BINDING SITE, designated SEQ ID:15322, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51827] Another function of VGAM1499 is therefore inhibition of PRO1768 (Accession NM_014099). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1768. S164 (Accession XM_027330) is another VGAM1499 host target gene. S164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by S164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of S164 BINDING SITE, designated SEQ ID:30481, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51828] Another function of VGAM1499 is therefore inhibition of S164 (Accession XM_027330). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with S164. SP329 (Accession NM_030793) is another VGAM1499 host target gene. SP329 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by SP329, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP329 BINDING SITE, designated SEQ ID:25097, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51829] Another function of VGAM1499 is therefore inhibition of SP329 (Accession NM_030793). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP329. LOC123443 (Accession XM_058707) is another VGAM1499 host target gene. LOC123443 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC123443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123443 BINDING SITE, designated SEQ ID:36725, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51830] Another function of VGAM1499 is therefore inhibition of

LOC123443 (Accession XM_058707). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123443. LOC130535 (Accession XM_072244) is another VGAM1499 host target gene. LOC130535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130535 BINDING SITE, designated SEQ ID:37476, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51831] Another function of VGAM1499 is therefore inhibition of LOC130535 (Accession XM_072244). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130535. LOC130813 (Accession XM_065904) is another VGAM1499 host target gene. LOC130813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC130813 BINDING SITE, designated SEQ ID:37311, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51832] Another function of VGAM1499 is therefore inhibition of LOC130813 (Accession XM_065904). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130813. LOC149301 (Accession XM_086480) is another VGAM1499 host target gene. LOC149301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149301 BINDING SITE, designated SEQ ID:38686, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51833] Another function of VGAM1499 is therefore inhibition of LOC149301 (Accession XM_086480). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149301. LOC164382 (Accession XM_104390) is an-

other VGAM1499 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42159, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51834] Another function of VGAM1499 is therefore inhibition of LOC164382 (Accession XM_104390). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC203523 (Accession XM_114713) is another VGAM1499 host target gene. LOC203523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203523 BINDING SITE, designated SEQ ID:43053, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51835] Another function of VGAM1499 is therefore inhibition of LOC203523 (Accession XM_114713). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203523. LOC85479 (Accession NM_033105) is another VGAM1499 host target gene. LOC85479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC85479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85479 BINDING SITE, designated SEQ ID:26958, to the nucleotide sequence of VGAM1499 RNA, herein designated VGAM RNA, also designated SEQ ID:4210.

[51836] Another function of VGAM1499 is therefore inhibition of LOC85479 (Accession NM_033105). Accordingly, utilities of VGAM1499 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85479. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1500 (VGAM1500) viral gene, which modulates expression of respective host target genes

thereof, the function and utility of which host target genes is known in the art.

[51837] VGAM1500 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1500 was detected is described hereinabove with reference to Figs. 1-8.

[51838] VGAM1500 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51839] VGAM1500 gene encodes a VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1500 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1500 precursor RNA is designated SEQ ID:1486, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1486 is located at position 3755 relative to the genome of Aphid Lethal Paralysis Virus.

[51840] VGAM1500 precursor RNA folds onto itself, forming VGAM1500 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51841] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1500 folded precursor RNA into VGAM1500 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM1500 RNA is designated SEQ ID:4211, and is provided hereinbelow with reference to the sequence listing part.

[51842] VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1500 host target RNA comprises three regions, as is typical of mRNA of a pro-

tein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51843] VGAM1500 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1500 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1500 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51844] The complementary binding of VGAM1500 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1500 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1500 host target RNA into VGAM1500 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51845] It is appreciated that VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1500 host target genes. The mRNA of each one of this plurality of VGAM1500 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1500 RNA, herein designated VGAM RNA, and which when bound by VGAM1500 RNA causes inhibition of translation of respective one or more VGAM1500 host target proteins.

[51846] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM1500 gene, herein designated VGAM GENE, on one or more VGAM1500 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51847] It is yet further appreciated that a function of VGAM1500 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1500 correlate with, and may be deduced from, the identity of the host target genes which VGAM1500 binds and inhibits, and the function of these host target genes, as

elaborated hereinbelow.

[51848] Nucleotide sequences of the VGAM1500 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1500 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1500 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1500 are further described hereinbelow with reference to Table 1.

[51849] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1500 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1500 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51850] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1500 gene, herein designated VGAM is inhibition of expression of VGAM1500 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1500 correlate with, and may be deduced from, the identity of the target genes which VGAM1500 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51851] Chromosome Condensation 1-like (CHC1L, Accession NM_001268) is a VGAM1500 host target gene. CHC1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHC1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHC1L BINDING SITE, designated SEQ ID:6932, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51852] A function of VGAM1500 is therefore inhibition of Chromosome Condensation 1-like (CHC1L, Accession NM_001268). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHC1L. Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM_004393) is another VGAM1500 host target gene. DAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAG1 BINDING SITE, designated SEQ ID:10632,

to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51853] Another function of VGAM1500 is therefore inhibition of Dystroglycan 1 (dystrophin-associated glycoprotein 1) (DAG1, Accession NM_004393), a gene which may provide linkage between the sarcolemma and extracellular matrix (ECM). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAG1. The function of DAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM1095.F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM_012308) is another VGAM1500 host target gene. FBXL11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXL11 BINDING SITE, designated SEQ ID:14681, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51854] Another function of VGAM1500 is therefore inhibition of F-box and Leucine-rich Repeat Protein 11 (FBXL11, Accession NM_012308), a gene which are BTB/POZ domain-containing zinc finger proteins implicated in oncogenesis. Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL11. The function of FBXL11 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM404. Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896) is another VGAM1500 host target gene. VPS26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VPS26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS26 BINDING SITE, designated SEQ ID:11327, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51855] Another function of VGAM1500 is therefore inhibition of Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896), a gene which is a sorting protein– ensures

the proper delivery of organelle-specific proteins. Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS26. The function of VPS26 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM315. KIAA0555 (Accession NM_014790) is another VGAM1500 host target gene. KIAA0555 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0555, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0555 BINDING SITE, designated SEQ ID:16684, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51856] Another function of VGAM1500 is therefore inhibition of KIAA0555 (Accession NM_014790). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0555. Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM_007150) is another VGAM1500 host target

gene. ZNF185 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF185, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF185 BINDING SITE, designated SEQ ID:14003, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51857] Another function of VGAM1500 is therefore inhibition of Zinc Finger Protein 185 (LIM domain) (ZNF185, Accession NM_007150). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF185. LOC115265 (Accession XM_055596) is another VGAM1500 host target gene. LOC115265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115265 BINDING SITE, designated SEQ ID:36309, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4211.

[51858] Another function of VGAM1500 is therefore inhibition of LOC115265 (Accession XM_055596). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115265. LOC257407 (Accession XM_173078) is another VGAM1500 host target gene. LOC257407 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257407 BINDING SITE, designated SEQ ID:46337, to the nucleotide sequence of VGAM1500 RNA, herein designated VGAM RNA, also designated SEQ ID:4211.

[51859] Another function of VGAM1500 is therefore inhibition of LOC257407 (Accession XM_173078). Accordingly, utilities of VGAM1500 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257407. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1501 (VGAM1501) viral gene, which

modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51860] VGAM1501 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1501 was detected is described hereinabove with reference to Figs. 1–8.

[51861] VGAM1501 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51862] VGAM1501 gene encodes a VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1501 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1501 precursor RNA is designated SEQ ID:1487, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1487 is located at position 1260 relative to the genome of Aphid Lethal Paralysis Virus.

[51863] VGAM1501 precursor RNA folds onto itself, forming

VGAM1501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51864] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1501 folded precursor RNA into VGAM1501 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM1501 RNA is designated SEQ ID:4212, and is provided hereinbelow with reference to the sequence listing part.

[51865] VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1501 host target RNA

comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[51866] VGAM1501 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1501 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1501 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51867] The complementary binding of VGAM1501 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1501 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1501 host target RNA into VGAM1501 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51868] It is appreciated that VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1501 host target genes. The mRNA of each one of this plurality of VGAM1501 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1501 RNA, herein designated VGAM RNA, and which when bound by VGAM1501 RNA causes inhibition of translation of respective one or more VGAM1501 host target proteins.

[51869] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM1501 gene, herein designated VGAM GENE, on one or more VGAM1501 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51870] It is yet further appreciated that a function of VGAM1501 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1501 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1501 correlate with, and may be deduced from, the identity of the host target genes which VGAM1501 binds and in-

hibits, and the function of these host target genes, as elaborated hereinbelow.

[51871] Nucleotide sequences of the VGAM1501 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1501 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1501 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1501 are further described hereinbelow with reference to Table 1.

[51872] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1501 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1501 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51873] As mentioned hereinabove with reference to Fig. 1, a function of VGAM1501 gene, herein designated VGAM is inhibition of expression of VGAM1501 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1501 correlate with, and may be deduced from, the identity of the target genes which VGAM1501 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[51874] Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152) is a VGAM1501 host target gene. C20orf12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf12 BINDING SITE, designated SEQ ID:19955, to the nucleotide sequence of VGAM1501 RNA, herein designated VGAM RNA, also designated SEQ ID:4212.

[51875] A function of VGAM1501 is therefore inhibition of Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152). Accordingly, utilities of VGAM1501 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf12. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1502 (VGAM1502) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51876] VGAM1502 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1502 was detected is described hereinabove with reference to Figs. 1–8.

[51877] VGAM1502 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51878] VGAM1502 gene encodes a VGAM1502 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1502 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1502 precursor RNA is designated SEQ ID:1488, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1488 is located at position 1441 relative to the genome of Aphid Lethal Paralysis Virus.

[51879] VGAM1502 precursor RNA folds onto itself, forming VGAM1502 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51880] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1502 folded precursor RNA into VGAM1502 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM1502 RNA is designated SEQ ID:4213, and is provided hereinbelow with reference to the sequence listing part.

[51881] VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1502 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[51882] VGAM1502 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1502 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1502 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51883] The complementary binding of VGAM1502 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1502 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1502 host target RNA into VGAM1502 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51884] It is appreciated that VGAM1502 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1502 host target genes. The mRNA of each one of this plurality of VGAM1502 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1502 RNA, herein designated VGAM RNA, and which when bound by VGAM1502 RNA causes inhibition of translation of respective one or more VGAM1502 host target proteins.

[51885] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1502 gene, herein designated VGAM GENE, on one or more VGAM1502 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51886] It is yet further appreciated that a function of VGAM1502 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1502 correlate with, and may be deduced from, the identity of the host target genes which VGAM1502 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51887] Nucleotide sequences of the VGAM1502 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1502 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1502 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1502 are further
described hereinbelow with reference to Table 1.

[51888] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1502 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1502 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[51889] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1502 gene, herein designated VGAM is
inhibition of expression of VGAM1502 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1502 correlate with, and may be deduced
from, the identity of the target genes which VGAM1502
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[51890] Desmocollin 1 (DSC1, Accession NM_024421) is a
VGAM1502 host target gene. DSC1 BINDING SITE1 and

DSC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSC1 BINDING SITE1 and DSC1 BINDING SITE2, designated SEQ ID:23660 and SEQ ID:11390 respectively, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51891] A function of VGAM1502 is therefore inhibition of Desmocollin 1 (DSC1, Accession NM_024421), a gene which is a component of intercellular desmosome junctions. Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSC1. The function of DSC1 has been established by previous studies. The desmosome is a complex adhesive structure that plays a fundamental role in maintaining the strength and integrity of epithelial tissues. Central to this role are transmembrane glycoproteins that mediate cell-cell adhesion at the extracellular surface and interact with the cytoskeleton (via components of the desmosomal plaque), thus linking the intermediate filament networks of adjacent cells. Desmosomal glycopro-

teins comprise 2 distinct groups, the desmogleins and the desmocollins, both of which are members of the cadherin superfamily of Ca^{2+} -dependent cell adhesion molecules. In the human, 2 types of desmocollins had been identified, symbolized DSC1 and DSC2 (OMIM Ref. No. 125645), and each occurs in 2 alternatively spliced forms (variants a and b) that have different cytoplasmic domains reflecting different interactions with components of the desmosomal plaque (Trojanovsky et al., 1993). King et al. (1993) isolated cDNA clones encoding a human desmocollin that is expressed in the more differentiated layers of human epidermis. This isoform has 53% amino acid identity with the previously isolated type 3 desmocollin, which is expressed in the basal layers of the epidermis. However, the N and C termini of the mature proteins are more highly conserved. Using a panel of somatic cell hybrids, King et al. (1993) assigned the DSC1 gene to chromosome 18, where the DSC2 gene and the 3 desmoglein genes (DSG1, 125670; DSG2, 125671; DSG3, 169615) had previously been mapped.

[51892] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [51893] King, I. A.; Arnemann, J.; Spurr, N. K.; Buxton, R. S. : Cloning of the cDNA (DSC1) coding for human type 1 desmocollin and its assignment to chromosome 18. *Genomics* 18: 185–194, 1993. ; and
- [51894] Troyanovsky, S. M.; Eshkind, L. G.; Troyanovsky, R. B.; Leube, R. E.; Franke, W. W. : Contributions of cytoplasmic domains of desmosomal cadherins to desmosome assembly and intermediate.
- [51895] Further studies establishing the function and utilities of DSC1 are found in John Hopkins OMIM database record ID 125643, and in cited publications numbered 359–360 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Replication Protein A1, 70kDa (RPA1, Accession NM_002945) is another VGAM1502 host target gene. RPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPA1 BINDING SITE, designated SEQ ID:8856, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51896] Another function of VGAM1502 is therefore inhibition of Replication Protein A1, 70kDa (RPA1, Accession NM_002945), a gene which is required for simian virus 40 dna replication in vitro. it participates in a very early step in initiation. rp-a is a single-stranded dna-binding protein. Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPA1. The function of RPA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM180. Tumor Necrosis Factor (ligand) Superfamily, Member 8 (TNFSF8, Accession NM_001244) is another VGAM1502 host target gene. TNFSF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF8 BINDING SITE, designated SEQ ID:6916, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51897] Another function of VGAM1502 is therefore inhibition of

Tumor Necrosis Factor (ligand) Superfamily, Member 8 (TNFSF8, Accession NM_001244), a gene which cytokine that binds to tnfrsf8/cd30. induces proliferation of t cells. Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF8. The function of TNFSF8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM655. BRAL1 (Accession NM_021817) is another VGAM1502 host target gene. BRAL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BRAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRAL1 BINDING SITE, designated SEQ ID:22395, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51898] Another function of VGAM1502 is therefore inhibition of BRAL1 (Accession NM_021817). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRAL1.

FLJ12838 (Accession NM_024641) is another VGAM1502 host target gene. FLJ12838 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12838, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12838 BINDING SITE, designated SEQ ID:23926, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51899] Another function of VGAM1502 is therefore inhibition of FLJ12838 (Accession NM_024641). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12838. HSPC067 (Accession NM_014158) is another VGAM1502 host target gene. HSPC067 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPC067, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC067 BINDING SITE, designated SEQ ID:15459, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM

RNA, also designated SEQ ID:4213.

[51900] Another function of VGAM1502 is therefore inhibition of HSPC067 (Accession NM_014158). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC067. KIAA1210 (Accession XM_172801) is another VGAM1502 host target gene. KIAA1210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1210 BINDING SITE, designated SEQ ID:46089, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51901] Another function of VGAM1502 is therefore inhibition of KIAA1210 (Accession XM_172801). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1210. KIAA1676 (Accession XM_167612) is another VGAM1502 host target gene. KIAA1676 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1676, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1676 BINDING SITE, designated SEQ ID:44730, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51902] Another function of VGAM1502 is therefore inhibition of KIAA1676 (Accession XM_167612). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1676. Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog 3 (mouse) (MEIS3, Accession XM_085721) is another VGAM1502 host target gene. MEIS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEIS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEIS3 BINDING SITE, designated SEQ ID:38310, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51903] Another function of VGAM1502 is therefore inhibition of Meis1, Myeloid Ecotropic Viral Integration Site 1 Homolog

3 (mouse) (MEIS3, Accession XM_085721). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEIS3. poly(rC) Binding Protein 4 (PCBP4, Accession NM_020418) is another VGAM1502 host target gene. PCBP4 BINDING SITE1 through PCBP4 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCBP4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCBP4 BINDING SITE1 through PCBP4 BINDING SITE3, designated SEQ ID:21679, SEQ ID:26894 and SEQ ID:26896 respectively, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51904] Another function of VGAM1502 is therefore inhibition of poly(rC) Binding Protein 4 (PCBP4, Accession NM_020418). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCBP4. Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM_006671) is another VGAM1502 host target gene. SLC1A7 BINDING SITE is HOST TARGET binding site found

in the 3` untranslated region of mRNA encoded by SLC1A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A7 BINDING SITE, designated SEQ ID:13492, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51905] Another function of VGAM1502 is therefore inhibition of Solute Carrier Family 1 (glutamate transporter), Member 7 (SLC1A7, Accession NM_006671). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A7. Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM_016598) is another VGAM1502 host target gene. ZDHHC3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZDHHC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC3 BINDING SITE, designated SEQ ID:18690, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4213.

[51906] Another function of VGAM1502 is therefore inhibition of Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM_016598). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC3. LOC157918 (Accession XM_098842) is another VGAM1502 host target gene. LOC157918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157918 BINDING SITE, designated SEQ ID:41901, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51907] Another function of VGAM1502 is therefore inhibition of LOC157918 (Accession XM_098842). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157918. LOC257468 (Accession XM_170838) is another VGAM1502 host target gene. LOC257468 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257468 BINDING SITE, designated SEQ ID:45625, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51908] Another function of VGAM1502 is therefore inhibition of LOC257468 (Accession XM_170838). Accordingly, utilities of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257468. LOC257486 (Accession XM_045029) is another VGAM1502 host target gene. LOC257486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257486 BINDING SITE, designated SEQ ID:34327, to the nucleotide sequence of VGAM1502 RNA, herein designated VGAM RNA, also designated SEQ ID:4213.

[51909] Another function of VGAM1502 is therefore inhibition of LOC257486 (Accession XM_045029). Accordingly, utilities

of VGAM1502 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257486. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1503 (VGAM1503) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51910] VGAM1503 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1503 was detected is described hereinabove with reference to Figs. 1-8.

[51911] VGAM1503 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51912] VGAM1503 gene encodes a VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1503 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nu-

cleotide sequence of VGAM1503 precursor RNA is designated SEQ ID:1489, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1489 is located at position 9098 relative to the genome of Aphid Lethal Paralysis Virus.

[51913] VGAM1503 precursor RNA folds onto itself, forming VGAM1503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51914] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1503 folded precursor RNA into VGAM1503 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM1503 RNA is designated SEQ ID:4214, and

is provided hereinbelow with reference to the sequence listing part.

[51915] VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1503 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[51916] VGAM1503 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1503 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM1503 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51917] The complementary binding of VGAM1503 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1503 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1503 host target RNA into VGAM1503 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51918] It is appreciated that VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1503 host target genes. The mRNA of each one of this plurality of VGAM1503 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com–

plementary to VGAM1503 RNA, herein designated VGAM RNA, and which when bound by VGAM1503 RNA causes inhibition of translation of respective one or more VGAM1503 host target proteins.

[51919] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1503 gene, herein designated VGAM GENE, on one or more VGAM1503 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51920] It is yet further appreciated that a function of VGAM1503 is inhibition of expression of host target genes, as part of

a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1503 correlate with, and may be deduced from, the identity of the host target genes which VGAM1503 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51921] Nucleotide sequences of the VGAM1503 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM1503 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM1503 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM1503 are further described hereinbelow with reference to Table 1.

[51922] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM1503 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM1503 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[51923] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM1503 gene, herein designated VGAM is inhibition of expression of VGAM1503 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM1503 correlate with, and may be deduced from, the identity of the target genes which VGAM1503 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[51924] Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is a VGAM1503 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28937, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51925] A function of VGAM1503 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1.

Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011) is another VGAM1503 host target gene. SOCS5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SOCS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOCS5 BINDING SITE, designated SEQ ID:15231, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51926] Another function of VGAM1503 is therefore inhibition of Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOCS5. ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM1503 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE,

designated SEQ ID:31075, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51927] Another function of VGAM1503 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. DKFZP434P0721 (Accession XM_033181) is another VGAM1503 host target gene. DKFZP434P0721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0721 BINDING SITE, designated SEQ ID:31869, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51928] Another function of VGAM1503 is therefore inhibition of DKFZP434P0721 (Accession XM_033181). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0721. KIAA1255 (Accession XM_040626)

is another VGAM1503 host target gene. KIAA1255 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1255, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1255 BINDING SITE, designated SEQ ID:33347, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51929] Another function of VGAM1503 is therefore inhibition of KIAA1255 (Accession XM_040626). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1255. RAB22A, Member RAS Oncogene Family (RAB22A, Accession XM_009454) is another VGAM1503 host target gene. RAB22A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB22A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB22A BINDING SITE, designated SEQ ID:30110, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:4214.

[51930] Another function of VGAM1503 is therefore inhibition of RAB22A, Member RAS Oncogene Family (RAB22A, Accession XM_009454). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB22A. LOC129607 (Accession XM_059368) is another VGAM1503 host target gene. LOC129607 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129607, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129607 BINDING SITE, designated SEQ ID:36975, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51931] Another function of VGAM1503 is therefore inhibition of LOC129607 (Accession XM_059368). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129607. LOC157918 (Accession XM_098842) is another VGAM1503 host target gene. LOC157918 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC157918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157918 BINDING SITE, designated SEQ ID:41893, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51932] Another function of VGAM1503 is therefore inhibition of LOC157918 (Accession XM_098842). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157918. LOC157919 (Accession XM_088420) is another VGAM1503 host target gene. LOC157919 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157919 BINDING SITE, designated SEQ ID:39680, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51933] Another function of VGAM1503 is therefore inhibition of LOC157919 (Accession XM_088420). Accordingly, utilities

of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157919. LOC219623 (Accession XM_166143) is another VGAM1503 host target gene. LOC219623 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219623, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219623 BINDING SITE, designated SEQ ID:43947, to the nucleotide sequence of VGAM1503 RNA, herein designated VGAM RNA, also designated SEQ ID:4214.

[51934] Another function of VGAM1503 is therefore inhibition of LOC219623 (Accession XM_166143). Accordingly, utilities of VGAM1503 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219623. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1504 (VGAM1504) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51935] VGAM1504 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1504 was detected is described hereinabove with reference to Figs. 1–8.

[51936] VGAM1504 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51937] VGAM1504 gene encodes a VGAM1504 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1504 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1504 precursor RNA is designated SEQ ID:1490, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1490 is located at position 8300 relative to the genome of Aphid Lethal Paralysis Virus.

[51938] VGAM1504 precursor RNA folds onto itself, forming VGAM1504 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51939] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1504 folded precursor RNA into VGAM1504 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM1504 RNA is designated SEQ ID:4215, and is provided hereinbelow with reference to the sequence listing part.

[51940] VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1504 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[51941] VGAM1504 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1504 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1504 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51942] The complementary binding of VGAM1504 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1504 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1504 host target RNA into VGAM1504 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51943] It is appreciated that VGAM1504 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1504 host target genes. The mRNA of each one of this plurality of VGAM1504 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1504 RNA, herein designated VGAM RNA, and which when bound by VGAM1504 RNA causes inhibition of translation of respective one or more VGAM1504 host target proteins.

[51944] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1504 gene, herein designated VGAM GENE, on one or more VGAM1504 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51945] It is yet further appreciated that a function of VGAM1504 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1504 correlate with, and may be deduced from, the identity of the host target genes which VGAM1504 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51946] Nucleotide sequences of the VGAM1504 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1504 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1504 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1504 are further
described hereinbelow with reference to Table 1.

[51947] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1504 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1504 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[51948] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1504 gene, herein designated VGAM is
inhibition of expression of VGAM1504 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1504 correlate with, and may be deduced
from, the identity of the target genes which VGAM1504
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[51949] GATA Binding Protein 2 (GATA2, Accession NM_002050) is
a VGAM1504 host target gene. GATA2 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE, designated SEQ ID:7805, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51950] A function of VGAM1504 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM_002050). Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. MGC2306 (Accession NM_032638) is another VGAM1504 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26355, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51951] Another function of VGAM1504 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863) is another VGAM1504 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11278, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51952] Another function of VGAM1504 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863). Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. LOC51014 (Accession XM_038077) is another VGAM1504 host target gene. LOC51014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC51014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51014 BINDING SITE, designated SEQ ID:32752, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51953] Another function of VGAM1504 is therefore inhibition of LOC51014 (Accession XM_038077). Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51014. LOC51213 (Accession NM_016383) is another VGAM1504 host target gene. LOC51213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51213 BINDING SITE, designated SEQ ID:18527, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51954] Another function of VGAM1504 is therefore inhibition of LOC51213 (Accession NM_016383). Accordingly, utilities

of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51213. LOC92399 (Accession NM_138777) is another VGAM1504 host target gene. LOC92399 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92399 BINDING SITE, designated SEQ ID:29011, to the nucleotide sequence of VGAM1504 RNA, herein designated VGAM RNA, also designated SEQ ID:4215.

[51955] Another function of VGAM1504 is therefore inhibition of LOC92399 (Accession NM_138777). Accordingly, utilities of VGAM1504 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92399. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 1505 (VGAM1505) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[51956] VGAM1505 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM1505 was detected is described hereinabove with reference to Figs. 1–8.

[51957] VGAM1505 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Aphid Lethal Paralysis Virus. VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[51958] VGAM1505 gene encodes a VGAM1505 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM1505 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM1505 precursor RNA is designated SEQ ID:1491, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1491 is located at position 8120 relative to the genome of Aphid Lethal Paralysis Virus.

[51959] VGAM1505 precursor RNA folds onto itself, forming VGAM1505 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the

art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[51960] An enzyme complex designated DICER COMPLEX, `dices` the VGAM1505 folded precursor RNA into VGAM1505 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM1505 RNA is designated SEQ ID:4216, and is provided hereinbelow with reference to the sequence listing part.

[51961] VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM1505 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated

5`UTR, PROTEIN CODING and 3`UTR respectively.

[51962] VGAM1505 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM1505 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM1505 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[51963] The complementary binding of VGAM1505 RNA, herein designated VGAM RNA, to host target binding sites on VGAM1505 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM1505 host target RNA into VGAM1505 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[51964] It is appreciated that VGAM1505 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM1505 host target genes. The mRNA of each one of this plurality of VGAM1505 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM1505 RNA, herein designated VGAM RNA, and which when bound by VGAM1505 RNA causes inhibition of translation of respective one or more VGAM1505 host target proteins.

[51965] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM1505 gene, herein designated VGAM GENE, on one or more VGAM1505 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[51966] It is yet further appreciated that a function of VGAM1505 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGAM1505 correlate with, and may be deduced from, the identity of the host target genes which VGAM1505 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[51967] Nucleotide sequences of the VGAM1505 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM1505 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM1505 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM1505 are further
described hereinbelow with reference to Table 1.

[51968] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM1505 host target RNA, and
schematic representation of the complementarity of each
of these host target binding sites to VGAM1505 RNA,
herein designated VGAM RNA, are described hereinbelow
with reference to Table 2.

[51969] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM1505 gene, herein designated VGAM is
inhibition of expression of VGAM1505 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM1505 correlate with, and may be deduced
from, the identity of the target genes which VGAM1505
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[51970] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase,
Polypeptide 3 (B3GALT3, Accession NM_033167) is a

VGAM1505 host target gene. B3GALT3 BINDING SITE1 and B3GALT3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT3 BINDING SITE1 and B3GALT3 BINDING SITE2, designated SEQ ID:27017 and SEQ ID:27020 respectively, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51971] A function of VGAM1505 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 3 (B3GALT3, Accession NM_033167). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT3. Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM_006731) is another VGAM1505 host target gene. FCMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of FCMD BINDING SITE, designated SEQ ID:13572, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51972] Another function of VGAM1505 is therefore inhibition of Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM_006731). Accordingly, utilities of VGAM1505 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCMD. V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog K (avian) (MAFK, Accession NM_002360) is another VGAM1505 host target gene. MAFK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAFK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAFK BINDING SITE, designated SEQ ID:8173, to the nucleotide sequence of VGAM1505 RNA, herein designated VGAM RNA, also designated SEQ ID:4216.

[51973] Another function of VGAM1505 is therefore inhibition of V-maf Musculoaponeurotic Fibrosarcoma Oncogene Homolog K (avian) (MAFK, Accession NM_002360), a gene